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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, 2016

OR

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

For the Transition Period from to

Commission File Number: 001-37708

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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ 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, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large Accelerated Filer	☐	Accelerated Filer	☐
Non-accelerated Filer	☒ (Do not check if a smaller reporting company)	Smaller Reporting Company	☐

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

As of June 30, 2016, 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 $109.6 million, based on the closing price of the registrant's common stock on June 30, 2016. 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 7, 2017, there were 18,244,423 shares of common stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement for its 2017 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, 2016, 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 lung cancer, melanoma, ovarian cancer and triple negative 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 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;
- the potential use of entinostat to treat additional tumor types, including head and neck, bladder and renal cells;
- our ability to maintain our licenses with Bayer Pharma AG, Kyowa Hakko Kirin Co., Ltd. and UCB Biopharma Sprl;
- 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 relating to our operations, results of operations, industry and future growth. 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, we cannot guarantee future results, levels of activity, performance or achievements. 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

We are a clinical stage biopharmaceutical company developing an innovative pipeline of combination therapies in multiple cancer indications. Our lead product candidate, entinostat, is currently being evaluated in a Phase 3 clinical trial for advanced hormone receptor positive, or HR+, human epidermal growth factor receptor 2 negative, or HER2-, breast cancer. Entinostat was granted Breakthrough Therapy designation by the U.S. Food and Drug Administration, or the FDA, following positive results from our Phase 2b clinical trial, ENCORE 301. We are developing entinostat, which has direct effects on both cancer cells and immune regulatory cells, and SNDX-6352, a monoclonal antibody that targets the colony stimulating factor-1 receptor, or CSF-1R, to enhance the body's immune response on tumors that have shown sensitivity to immunotherapy. We acquired the exclusive rights to SNDX-6352 in July 2016 and are evaluating entinostat as a combination therapeutic in Phase 1b/2 clinical trials with Merck & Co., Inc., or Merck, for non-small cell lung cancer and melanoma; with Genentech, Inc., or Genentech, for triple negative breast cancer, or TNBC; and with Merck KGaA, Darmstadt, Germany, or Merck KGaA, and Pfizer Inc., or Pfizer, for ovarian cancer. We are evaluating SNDX-6352 in a single ascending dose Phase 1 clinical trial. 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.

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 1,000 cancer patients. We believe that, based on its mechanism of action, entinostat may have broad applications in additional tumor types, including head and neck, bladder and renal cell, which are immuno-responsive, or sensitive to immunotherapy.

Immuno-oncology is an emerging field of cancer medicine that has focused on the development of therapeutic approaches designed to activate the immune system to find and destroy cancer cells. Many tumors have the ability to evade the immune system through direct cellular interactions and recruitment of immuno-suppressive cells to the area surrounding the tumor. One such evasion mechanism is through the expression of proteins known as checkpoint proteins, such as programmed cell death protein ligand 1, or PD-L1, on the cancer cell surface. These checkpoint proteins bind to a corresponding receptor known as programmed cell death protein 1, or PD-1, which is expressed on particular immune cells known as cytotoxic T cells. Through this binding process, cytotoxic T cells are blocked from killing cancer cells. Antibodies known as immune checkpoint inhibitors block the interaction between PD-1 and PD-L1 to restore the ability of cytotoxic T cells to kill cancer cells and have shown significant clinical benefit in treating certain cancers. We believe that entinostat acts on a different tumor-evasion mechanism than is targeted by most other immunotherapies in development. Instead of focusing on the interaction between the T cell and the tumor, 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.

We believe entinostat, a Class 1-specific histone deacetylase, or HDAC, inhibitor, is the therapy most advanced in development that can directly reduce both the number and activity of MDSCs and Tregs 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. Through this important effect on MDSCs and Tregs, entinostat has the potential to be used synergistically with therapies working to stimulate the immune system. The long half-life of entinostat allows for continuous exposure to therapy potentially resulting in positive immuno-modulatory effects 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.

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., tumor-associated macrophages or 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.

SNDX-6352 is an immunoglobulin G subclass 4, or IgG4, isotype that binds to the ligand binding domain of CSF-1R, blocking the binding and consequent activation by both natural ligands interleukin-34, or IL-34, and colony stimulating factor-1, or CSF-1, and disrupting TAM activity. We believe that the Ig subtype may provide differentiation in terms of safety and/or efficacy of the antibodies as single agent or in combinations. It is through this mechanism that we believe SNDX-6352 can decrease the ability of the tumor to grow and spread to other parts of the body. 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.

Our Strategy

We are focused on developing entinostat and SNDX-6352 to enhance the body's immune response on tumors that have shown sensitivity to immunotherapy, as well as developing entinostat for use in multiple cancer indications in combination with complementary therapeutic drugs. Key elements of our strategy include:

- Establish entinostat as the combination therapy of choice with immune checkpoint inhibitors, initially PD-1 and PD-L1 inhibitors. Our near-term focus is to rapidly establish proof of concept that entinostat can provide additional meaningful clinical benefit to patients in one or more tumor types when combined with a PD-1 inhibitor or a PD-L1 inhibitor. Our approach is to conduct clinical trials in patients with tumor types that are known to be responsive to PD-1 or PD-L1 inhibitors, such as NSCLC, melanoma, TNBC, ovarian cancer, head and neck cancer, bladder cancer and renal cell cancer. To that end, we have entered into non-exclusive collaborations with Merck, Genentech, and Merck KGaA and Pfizer. We intend to expand the existing collaborations or enter into additional collaborations through non-exclusive, clinical development agreements in order to assess entinostat's impact across multiple tumor types while maintaining our ownership rights.
- Pursue regulatory approval of entinostat in indications with significant unmet need and commercial potential. Assuming that one or more of our Phase 1b/2 clinical trials are successful, we expect to conduct clinical trials that may lead to accelerated approval and/or conduct pivotal Phase 3 clinical trials, which would serve as the basis of approval from the FDA and the European Commission. We may also seek breakthrough therapy designation from the FDA depending on the magnitude of the clinical benefit observed. The order in which we choose to pursue FDA approvals will depend on the results of the entinostat proof-of-concept clinical trials, the relative speed to FDA approval for any given indication, the unmet need that exists within any given patient population and the competitive landscape of other therapies approved or in development for a given indication.
- 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 Aromasin in advanced HR+ breast cancer. We believe that the submission of the results of the Phase 3 clinical trial, if successful, would be sufficient for regulatory approval of entinostat in the United States.
- Develop SNDX-6352 as a single agent and in combination in one or more tumor types. SNDX-6352 inhibits 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

TAMs and enable an immune response against tumors. Our near-term focus is rapidly establishing 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 commenced a single ascending dose Phase 1 clinical trial during the fourth quarter of 2016. We intend to conduct clinical trials in patients with tumor types having clear unmet needs and where we believe that the inhibition of TAMs via CSF-1R inhibition will synergize with the current standard of care, inducing tumor regressions.

- 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. Our management team, advisors and scientific collaborators are or have been affiliated with some of the world's leading research and development organizations and have a distinguished track record in product licensing, acquisitions and oncology drug development. We acquired the exclusive rights to SNDX-6352 in July 2016 and we intend to continue leveraging the collective talent within our organization and network of advisors to guide our pipeline expansion and development plans.

Clinical Development Programs

The following table sets forth information pertaining to our principal clinical trials for (1) entinostat with our initial focus on advancing ENCORE 601, ENCORE 602 and ENCORE 603 in immuno-oncology and (2) entinostat in E2112, our collaboration with ECOG-ACRIN and the NCI, in HR+, HER2- breast cancer and (3) SNDX-6352 in immuno-oncology.

Entinostat						
Immuno-oncology	**Preclin.**	**Ph. 1**	**Ph. 2**	**Ph. 3**	**Indication(s)**	**Sponsor**
ENCORE 601: Entinostat + *KEYTRUDA®*					NSCLC / Melanoma	Syndax[1]
ENCORE 602: Entinostat + *TECENTRIQ®*					TNBC	Syndax[2]
ENCORE 603: Entinostat + avelumab					Ovarian Cancer	Syndax[3]
Advanced HR+, HER2- Breast Cancer						
E2112: Entinostat + *AROMASIN®*					Adv. HR+, HER2- Breast Cancer	NCI[4] / Syndax
Other						
Additional NCI- and investigator-sponsored studies are ongoing or planned in a variety of tumor types						

SNDX-6352						
Immuno-oncology	**Preclin.**	**Ph. 1**	**Ph. 2**	**Ph. 3**	**Indication(s)**	**Sponsor**
SNDX-6352-0001: Single ascending dose					Solid Tumors	Syndax[5]

(1) Conducted pursuant to an Investigational New Drug, or IND, application, which was filed with the FDA by Syndax Pharmaceuticals, Inc. on April 20, 2015.

(2) Conducted pursuant to an IND application, which was filed with the FDA by Syndax Pharmaceuticals, Inc. on January 26, 2016.
(3) Conducted pursuant to an IND application, which was filed with the FDA by Syndax Pharmaceuticals, Inc. on September 1, 2016.
(4) Conducted pursuant to an IND application, which was filed with the FDA by the NCI on October 24, 2013.
(5) This trial is in the planning phase and as such an IND has not yet been filed.

Cancer is a complex, often fatal, disease arising from uncontrolled cell growth and the ability of cancer cells to avoid the immune system, the body's primary defense mechanism for finding and destroying such cells. We are developing entinostat, which has direct effects on both cancer cells and immune regulatory cells. We have demonstrated that the delivery of entinostat in combination with hormone therapy can result in improvements in overall survival in advanced HR+ breast cancer patients. Entinostat has also demonstrated synergistic anti-tumor activity in combination with immune checkpoint inhibitors in preclinical studies. Entinostat is an oral, small molecule HDAC inhibitor. HDACs are enzymes that are subdivided into four classes and are known to play a role in controlling cell survival, proliferation, angiogenesis and immunity. While most HDAC inhibitors broadly inhibit multiple classes of HDACs, preclinical studies have shown that entinostat's inhibitory activity is selective to Class 1 HDACs, which have been shown to impact the number and activity of MDSCs and Tregs. We believe that entinostat's Class 1 selectivity enhances immune responses against cancer and is likely to lead to a better tolerability and combinability profile.

Entinostat is currently being studied in clinical trials across a broad range of solid tumors, including breast cancer, NSCLC and melanoma. We are working in collaboration with Merck to study the combination of entinostat with Merck's immune checkpoint inhibitor, *Keytruda*® (pembrolizumab), in a Phase 1b/2 clinical trial (ENCORE 601) of up to 158 patients with NSCLC or melanoma. The Phase 1b portion of the clinical trial evaluated the safety and tolerability of the combination of entinostat and *Keytruda* and has progressed to the Phase 2 portion of the clinical trial, which is assessing the safety and efficacy of entinostat combined with *Keytruda* in patients with either advanced metastatic or recurrent NSCLC or melanoma. Patient enrollment in the Phase 2 portion was initiated in October 2016. We have also entered into a collaboration with Genentech, Inc., or Genentech, to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with Genentech's immune checkpoint inhibitor, *Tecentriq*® (atezolizumab), in a Phase 1b/2 clinical trial (ENCORE 602) of patients with TNBC. Patient enrollment in the Phase 1b portion was completed in November 2016 and the Phase 2 portion of the trial was opened in December. We have also entered into a collaboration with Ares Trading, S.A., a subsidiary of Merck KGaA, Pfizer to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with the investigational monoclonal antibody targeting PD-L1, avelumab, in a Phase 1b/2 clinical trial, ENCORE 603, of patients with ovarian cancer. Avelumab is the proposed international non-proprietary name for the anti-PD-L1 IgG1 monoclonal antibody (MSB0010718C). We initiated ENCORE 603 in January 2017 and expect safety data from the Phase 1b safety portion during the first half of 2017. Additionally, entinostat is being evaluated in two 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.

Entinostat is also being evaluated in an ongoing Phase 3 clinical trial testing *Aromasin* in combination with entinostat versus *Aromasin* in combination with a placebo in patients with advanced HR+, HER2- breast cancer. ECOG Network Cancer Research Group, or ECOG-ACRIN, is conducting this clinical trial under sponsorship and funding support from the National Cancer Institute, or NCI. We are providing financial and operational support for this Phase 3 clinical trial under separate agreements with the NCI and ECOG-ACRIN. 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. The Phase 3 clinical trial is designed to determine whether the addition of entinostat to *Aromasin* improves progression-free survival, or PFS, overall survival, or both in patients who have previously progressed after treatment with standard-of-care hormonal agents. We believe that the submission of

the results of the Phase 3 clinical trial, if successful, would be sufficient for regulatory approval of entinostat in the United States.

We are also developing SNDX-6352, which we believe may enhance the body's immune response on tumors that have shown sensitivity to immunotherapy. With our entinostat program we have identified that many tumors have the ability to evade both the innate and adaptive immune system through direct cellular interactions and recruitment of immuno-suppressive cells such as MDSCs and Tregs to the area surrounding the tumor. Research has identified a third type of immuno-suppressive cell, known as a TAM, that is also recruited to the area surrounding the tumor and, together with MDSCs and Tregs, plays a significant role in helping a tumor evade detection and elimination by the immune system. TAMs are believed to play at least two key roles in promoting tumor cell growth. The first is to block the activity of those T cells that mediate the ability of the immune response to kill the tumor cell. The second is to secrete certain growth factors that induce the tumor cells to divide. Similar to MDSCs and Tregs, high levels of TAMs have been shown to correlate with poor prognosis for certain cancers and preclinical studies have demonstrated that inhibition of TAMs can enhance anti-tumor immune responses.

Investigation into how TAMs are formed and recruited to the area surrounding the tumor has discovered that TAMs express on their cell surface a receptor known as CSF-1R that controls their growth. CSF-1R activity is regulated by two molecules, CSF-1 and IL-34, that have been shown by researchers to bind directly to CSF-1R. Studies show that blocking both CSF-1 and IL-34 may be required in order to fully block signaling through CSF-1R and reduce the number and function of TAMs. SNDX-6352 is an IgG4 isotype that binds to the ligand binding domain of CSF-1R, blocking the binding and consequent activation by both IL-34 and CSF-1 and disrupting TAM activity.

SNDX-6352 is being evaluated in a single ascending dose Phase 1 clinical trial we commenced in the fourth quarter of 2016. We intend to conduct clinical trials in patients with tumor types having clear unmet needs and where we believe that the inhibition of TAMs via CSF-1R inhibition will synergize with the current standard of care, inducing tumor regressions.

Immuno-Oncology

Background

Immuno-oncology is an emerging field of cancer medicine that has focused on the development of therapeutic approaches designed to activate the immune system to find and destroy cancer cells. The immune system consists of two parts, the innate immune system and the adaptive immune system and both play a role in an effective anti-tumor immune response. The innate immune system, composed of key cells such as natural killer cells and neutrophils, is non-specific and is designed to rapidly identify and eliminate immediate threats to the body, such as infections and other pathogens. The adaptive immune system, composed of B cells, T cells and other immune regulatory cells, targets specific antigens and provides a long-term immune response, known as immunologic memory, to antigens it recognizes as foreign.

Many tumors have the ability to evade both the innate and adaptive immune system through direct cellular interactions and recruitment of immuno-suppressive cells to the area surrounding the tumor. Cancer cells can express proteins on their cell surface known as checkpoint proteins, such as PD-L1 and programmed cell death protein ligand 2, or PD-L2, that block the ability of immune cells known as cytotoxic T cells to kill cancer cells. Antibodies that block PD-L1 or PD-L2 restore the ability of cytotoxic T cells to kill cancer cells and have shown significant clinical benefit. Positive results notwithstanding, durable responses following treatment with immune checkpoint inhibitors have only been observed in a relatively small population of treated patients, with overall response rates falling below 30% depending on tumor type, and suggest that additional strategies enhancing the anti-tumor immune response are needed to improve the survival of cancer patients.

Research to identify the basis for the limited efficacy of recently developed immune therapies has provided investigators with an appreciation for the role that specific immune regulatory cells, such as MDSCs and Tregs, have in blocking the cytotoxic T cell response. MDSCs and Tregs localize in the area surrounding the tumor and, together with the immune checkpoints, play a significant role in helping a tumor evade detection and elimination by the immune system.

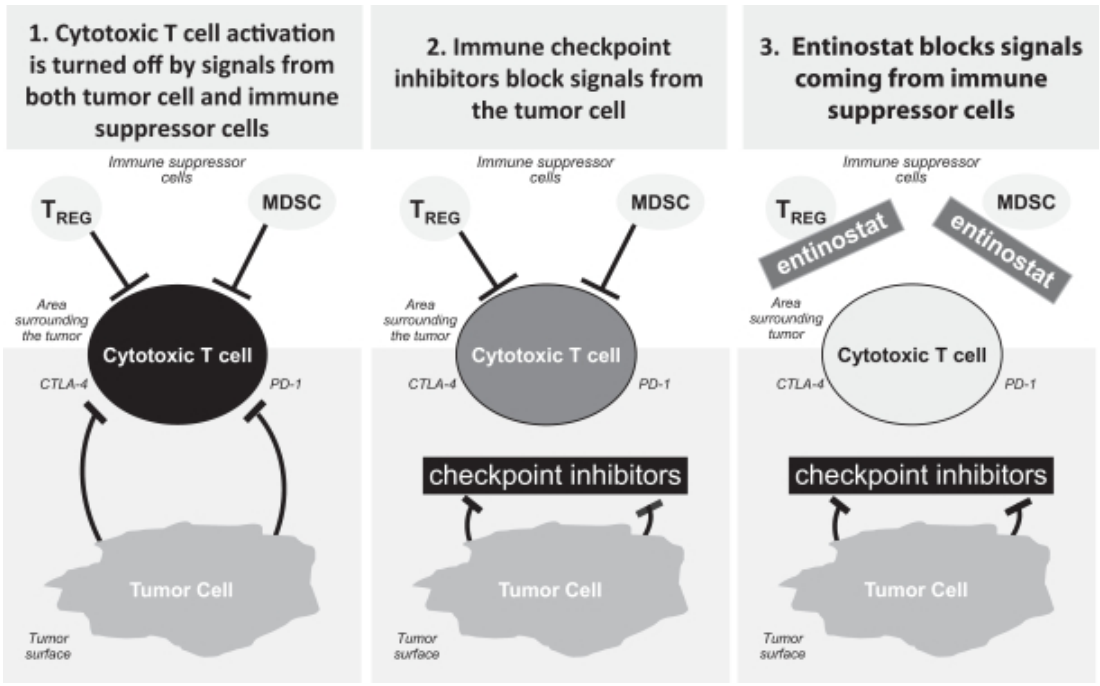
MDSCs are a group of immature myeloid cells that are activated by disease or injury and are generally increased in cancer patients. The primary function of MDSCs is to suppress an activated T cell immune response through the production and secretion of enzymes, which deplete key amino acids required for the growth and function of cytotoxic T cells. High levels of circulating MDSCs in various cancers, including breast, lung and head and neck, and others correspond with a poor prognosis and limited response to cancer therapy. Recent data further indicates that high levels of circulating MDSCs in melanoma patients are inversely correlated with clinical response to immune checkpoint inhibitors suggesting that targeting MDSCs may offer new therapeutic opportunities that enhance the anti-tumor response to immune checkpoint inhibitors.

Tregs are immune suppressor cells that are recruited to sites of active immune response in order to shut down the cytotoxic T cell response. A defining feature of immunosuppressive Tregs is the expression of a protein called FoxP3, or forkhead box p3. We refer to FoxP3+ Tregs as Tregs. Unlike MDSCs, which are found in activated states in circulating blood, Tregs may be recruited to the area surrounding the tumor and activated by local signals from the cancer cell. As with MDSCs, an increase in the level of activated Tregs correlates with poor prognosis in a number of tumor types including breast, colorectal, ovarian and other cancers. Tregs suppress cytotoxic T cell responses through the secretion of cytokines that inhibit the growth of cytotoxic T cells. In addition, Tregs can cause other immune regulatory cells in the area surrounding the tumor to secrete immune suppressive enzymes. Inhibiting Tregs may therefore relieve immune suppression in a way similar and potentially complementary to that of other immune-targeted approaches.

Entinostat as Immunotherapy

Preclinical and clinical data combined with the safety data observed in treating more than 1,000 cancer patients to date support our belief that entinostat has the potential to enhance the efficacy of immune checkpoint inhibitors across multiple tumor types. Entinostat is a Class 1-specific HDAC inhibitor targeting those HDACs shown to impact the number and activity of MDSCs and Tregs. We believe that entinostat acts on a different tumor-evasion mechanism than that being targeted by most other immunotherapies in development and is the most advanced agent that can directly reduce both the number and activity of MDSCs and Tregs while sparing the cytotoxic T cells. This impact of entinostat’s effect is presented in Figure 1 below, which illustrates how this mechanism can be highly complementary to immune checkpoint inhibitors.

Figure 1.



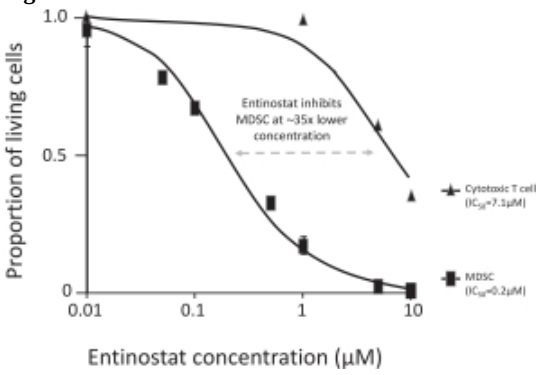
Source: Syndax

Data Supporting Entinostat as a Dual Inhibitor of Immune Suppressor Cells

Separate preclinical studies from investigators at Johns Hopkins University, or JHU, and Roswell Park Cancer Center have demonstrated that entinostat is a dual inhibitor of immune suppressor cells through its targeting of both MDSCs and Tregs. Figure 2 below shows that entinostat reduces the growth of MDSCs at concentrations that spare the growth of cytotoxic T cells. Approximately half of the MDSCs are stopped from growing at 200 nM of entinostat, which is 35 times less than the concentration of entinostat that stops half of the cytotoxic T cells from growing. Figure 3 shows that entinostat can also inhibit MDSC function. In this experiment the investigators mixed MDSCs with cytotoxic T cells and determined the level of T cell activity by measuring secreted amounts of interferon-gamma, a cytokine that is important for the anti-tumor immune

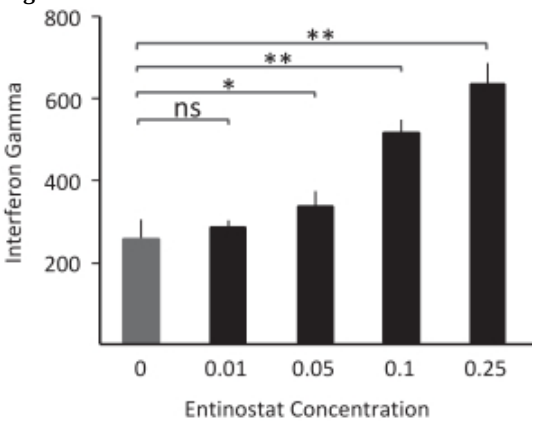
response. Adding increasing amounts of entinostat results in higher levels of interferon-gamma secretion indicating that entinostat is enhancing cytotoxic T cell activation by blocking MDSC suppression.

Figure 2.



Source: Kato et al 2007 American Association for Cancer Research

Figure 3.



Source: Adapted from Shen et al 2012 Public Library of Science

Entinostat has also been shown to inhibit Treg activity in preclinical experiments. As shown in Figures 4 and 5 below, investigators have used an animal model of renal cell carcinoma called RENCA in order to demonstrate that entinostat could block Treg-mediated immune suppression in order to enhance the activity of *Proleukin*® (aldesleukin) an approved immune therapy for renal cell carcinoma. In Figure 4, the shaded areas on the mice indicate tumor growth, and the size of individual tumors at the end of the study can be seen below each mouse. In this experiment, entinostat alone has some anti-tumor activity and when combined with *Proleukin* results in a significant reduction in the growth and size of the tumors. The graph in Figure 5 shows that *Proleukin* alone increases the levels of Tregs as a consequence of its immune activity and that entinostat alone, and in combination with *Proleukin*, blocks the increase in Tregs and reduces the number of immune-suppressive Tregs that are present in the tumor. In addition to reducing the number of immune-suppressive Tregs in this study, entinostat also increases the number of activated cytotoxic T cells.

Figure 4.

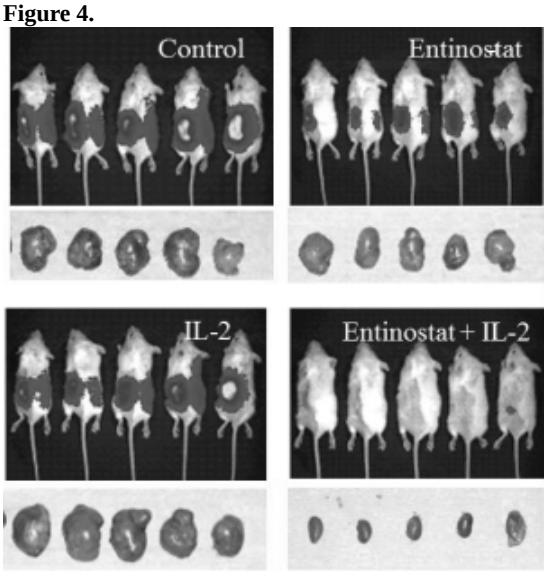
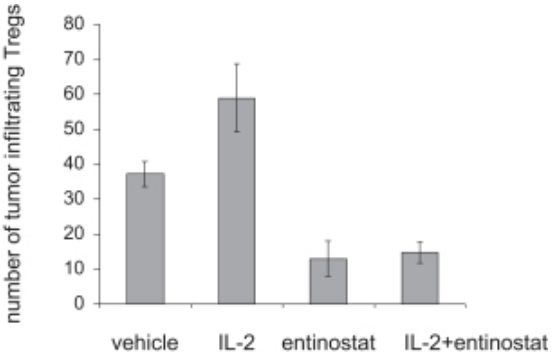
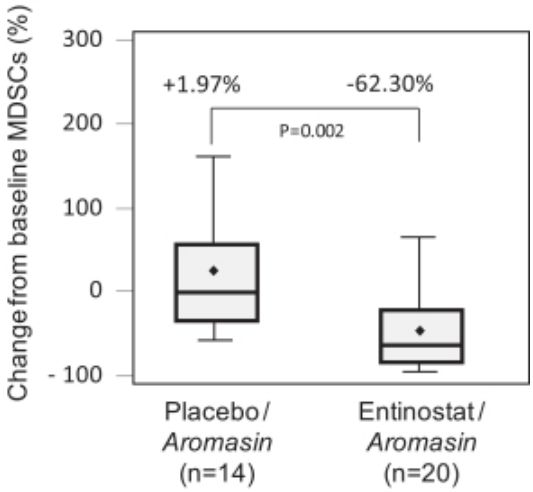


Figure 5.



In order to determine whether the effect of entinostat observed in preclinical research studies can also be observed in cancer patients treated with entinostat, we conducted an analysis on immune cells found in blood samples collected from a subset of patients treated in ENCORE 301, our Phase 2b clinical trial in advanced HR+ breast cancer patients. As shown in Figure 6 below, in these peripheral blood samples, we observed a statistically significant reduction in the level of circulating MDSCs in patients treated with the combination of entinostat and *Aromasin*, a hormone therapy, but not in patients treated with the combination of placebo and *Aromasin*. We believe this data collected from a subset of the ENCORE 301 patient population provided the first clinical evidence of entinostat-mediated reduction of immunosuppressive MDSCs in patients and is consistent with the impact on MDSCs observed in the preclinical animal studies.

Figure 6.



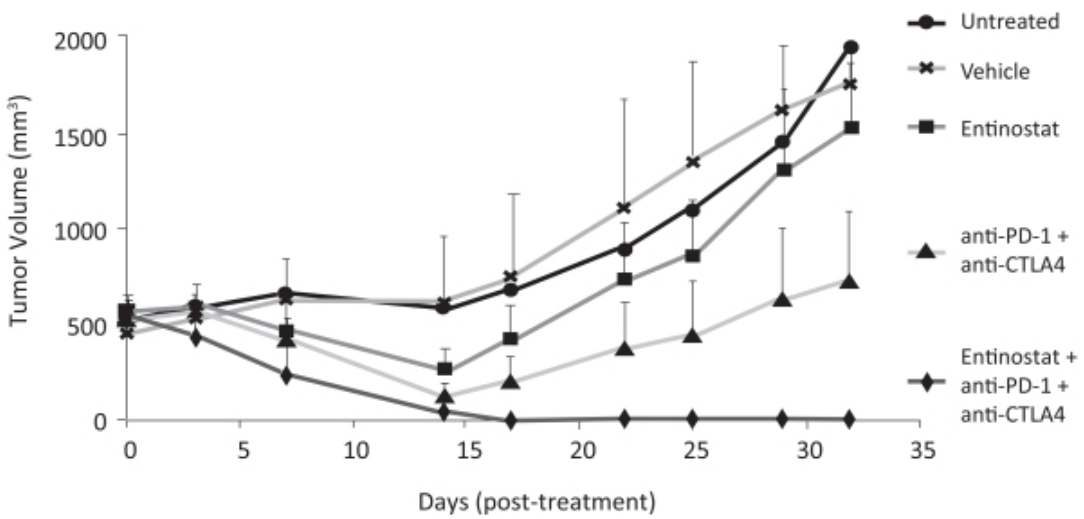
Source: Syndax

Data Supporting Entinostat in Combination with Immune Checkpoint Inhibitors

Preclinical. In order to determine whether entinostat could combine effectively with immune checkpoint inhibitors, investigators from JHU tested entinostat in combination with anti-PD-1 and anti-cytotoxic T-lymphocyte-associated protein 4, or CTLA4, directed antibodies in immune-resistant animal models. As shown in Figure 7 below, the elimination of both primary and metastatic tumors was observed in a 4T1 mouse breast cancer model that was treated with entinostat together with dual PD-1/CTLA4 checkpoint inhibition. The

researchers observed that entinostat, rather than attacking and destroying replicating cells as standard chemotherapy drugs do, reduced the number and activity of MDSCs.

Figure 7.

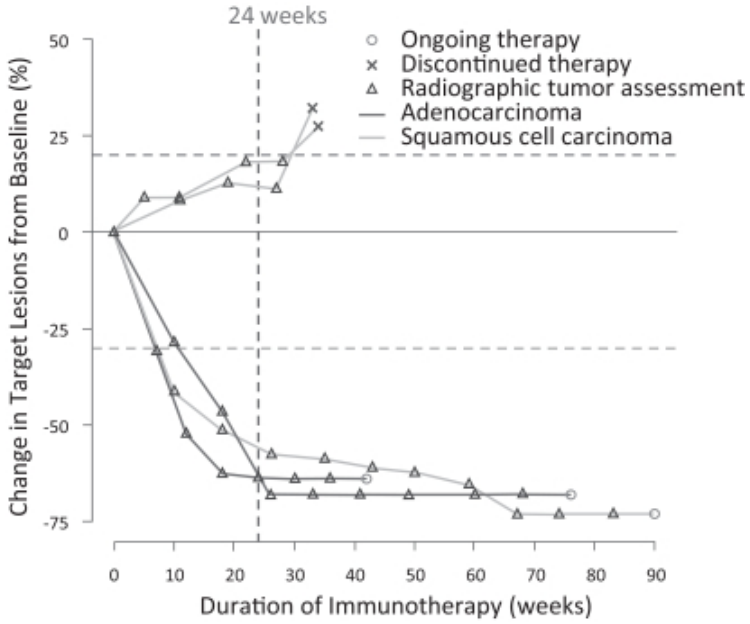


Source: Adapted from Kim et al 2014 Proceedings of the National Academy of Sciences

Clinical. Based on the clinical outcome of patients who were treated in two unrelated clinical trials, physicians at JHU observed preliminary evidence for the potential beneficial effects of combining entinostat with a PD-1 or PD-L1 inhibitor. In a heavily pre-treated metastatic NSCLC population, patients given the combination of entinostat and *Vidaza*® (azacitidine), an approved chemotherapeutic drug, achieved few objective responses and only a modest 4% overall response rate. However, investigators observed that these same patients who received the combination of entinostat and *Vidaza* and who subsequently received immune checkpoint therapy demonstrated a higher response rate than that expected for this patient population. Figure 8 below illustrates that all five patients who received either *Opdivo*®, an approved anti-PD-1, or an investigational PD-L1 inhibitor as their next therapy derived durable clinical benefit. Three of the patients had durable responses and two had durable stable disease. This enhanced response rate was better than an expected 15% response to *Opdivo* alone observed in a similar advanced NSCLC population and led investigators to hypothesize that the prior effect of the combination of entinostat and *Vidaza* therapy was “priming” the tumors to the subsequent immune therapy. To confirm these findings and further explore the ability of the combination of *Vidaza* and entinostat to enhance the

response of NSCLC patients to *Opdivo*, the investigators at JHU have initiated a follow-on randomized Phase 2 clinical trial, J1353.

Figure 8.



Source: Adapted from Wrangle et al 2013 Oncotarget

Entinostat with Immune Checkpoint Inhibitors in NSCLC and Melanoma

Market Overview and Current Treatment—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 will be diagnosed and an estimated 155,870 people will die from lung cancer in the United States. The five-year survival rate for patients with NSCLC generally is 18% and for patients with Stage III/IV NSCLC is approximately 6%, indicating a significant need for new therapies that can prolong overall survival.

Advanced metastatic NSCLC is a severe disease with a poor prognosis in the majority of patients with limited treatment options to date. Treatment typically includes a first-line combination chemotherapy followed by a choice of a second-line therapeutic approach. Most patients receiving first-line chemotherapy will relapse within one year of treatment with a median PFS of approximately five to six months and median overall survival of approximately 10 to 12 months. In the second-line setting, the median PFS is approximately three to four months and median overall survival is approximately six to seven months.

The treatment paradigm of NSCLC has been changing significantly since early 2015 when the FDA approved *Opdivo*, an anti-PD-1 monoclonal antibody as the first immune-targeted drug to treat people with squamous NSCLC in patients who have relapsed after platinum-based chemotherapy. Since the approval of *Opdivo* (nivolumab), two additional check point inhibitors. Tecentriq a PD-L1 antibody from Roche/Genentech, and Keytruda, a PD-1 antibody from Merck, have also been approved as a treatment for both squamous and nonsquamos NSCLC patients after use of platinum-based chemotherapy. The efficacy data observed with these

agents represents a significant increase from what has traditionally been expected of drugs approved to treat advanced NSCLC, and we believe that immune checkpoint inhibitors have become the standard of care for this patient population. Keytruda has also demonstrated an improvement over standard platinum-based chemotherapy in patients with advanced NSCLC, with ³50% PD-L1 expression in their tumors that had not received prior systemic treatment for advanced NSCLC.

There are other PD-L1 inhibitors being developed to treat NSCLC, including AstraZeneca plc's durvalumab (MEDI4736), and Merck KGaA /Pfizer's avelumab. The clinical development programs for all of these therapies have been designed to understand the broad impact they could have across NSCLC, including chemotherapy-naive and previously treated 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 (15 to 20%). 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.

Market Overview and Current Treatment—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 immuno-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*, 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.

Our Development of Entinostat in NSCLC and Melanoma

We have a clinical collaboration underway with Merck to study the safety and efficacy of entinostat in combination with *Keytruda* in patients with NSCLC and malignant melanoma. The ENCORE 601 clinical trial is a Phase 1b/2 clinical trial. The Phase 1b portion evaluated the safety, tolerability and biomarker correlates of the combination of entinostat and *Keytruda* in patients with NSCLC. The Phase 2 portion is assessing both the safety and efficacy of entinostat combined with *Keytruda* in patients with NSCLC and melanoma. The trial is an open label, dose escalation study with cohort expansions at the recommended Phase 2 dose, or RP2D, in NSCLC and melanoma patients. We are conducting the trial in the United States and will enroll 158 patients with 22 of those having been enrolled in the Phase 1b portion and approximately 136 of those to be enrolled in the Phase 2 portion. We announced safety data and RP2D data from the Phase 1b portion in the first half of 2016 and in the second half of 2016, respectively. Patient enrollment in the Phase 2 portion was initiated in October 2016, and we expect final efficacy data in 2018.

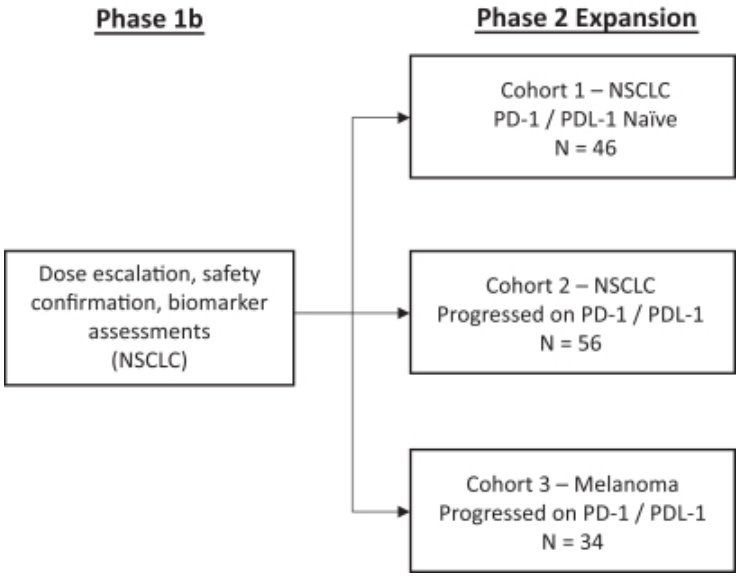
The primary objective of the Phase 1b portion of the trial was to determine the dose-limiting toxicities, or DLT, maximum tolerated dose, or MTD, or the RP2D of entinostat given in combination with *Keytruda*. The

initial three patients in Cohort 1 received weekly oral entinostat at a starting dose of 3 mg along with *Keytruda* 200 mg via intravenous infusion. Enrollment in Cohort 1 was increased to six patients after one of the initial three patients developed a serious immune-mediated adverse event. The patient in question developed Grade 3 elevations in alkaline phosphatase and serum bilirubin, which were considered to be manifestations of immune-mediated hepatitis. Immune-mediated hepatitis is included in the *Keytruda* U.S. Prescribing Information as a potential adverse drug reaction. The adverse event was successfully managed by withholding study drugs and administering systemic corticosteroids, leading to a rapid normalization of the abnormal laboratory values and resolution of symptoms. Based on a thorough safety review of all six patients, which demonstrated no similar events or any other dose-limiting toxicities, the 3 mg dosing was deemed tolerable; and in December 2015, dosing was escalated to entinostat weekly oral doses of 5 mg, which enrolled seven patients. The prospective RP2D was confirmed in nine additional patients. 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.

In the Phase 2 portion of the clinical trial, we are evaluating entinostat in combination with *Keytruda* using the RP2D identified in the Phase 1b portion with the primary objective of evaluating the efficacy of the combination in three expansion cohorts. In each cohort we are using a two-stage design in which a defined minimum number of responders must be seen in the first stage in order for the cohort to advance to full enrollment in the second stage. We have recently completed enrollment of the three cohorts in the first stage of the Phase 2 portion in patients with NSCLC and melanoma and therefore have closed enrollment for these cohorts. 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. In February 2017, the melanoma cohort of the 601 trial met the pre-specified objective response threshold; and we progressed to the second stage of the trial. This cohort will now enroll an additional 21 patients**.** Data from the other two cohorts, which will determine whether or not they continue onto Stage 2, is still maturing and is expected in the first half of 2017. If the pre-specified level of objective response is achieved and we reopen enrollment, Cohort 1 will enroll up to 46 NSCLC patients with any histology who have not previously been treated with a PD-1/PD-L1 inhibitor. We anticipate all 46 patients would be enrolled by the end of the second half of 2017. If the prescribed level of objective response is achieved and we reopen enrollment, Cohort 2 will enroll up to 56 patients with NSCLC of any histology who have previously been treated and progressed on a PD-1 or PD-L1 blocking antibody. We anticipate that all 56 patients would be enrolled by the end of the second half of 2017. Cohort 3 is enrolling up to 34 patients with melanoma who have previously been treated and progressed on a PD-1 or PD-L1 blocking antibody. We anticipate all 34 patients will be enrolled by the end of the second half of 2017.

Secondary objectives of the trial include assessments of safety, efficacy as measured by clinical benefit rate at six months, PFS at six months, overall PFS, overall survival, duration of response and time to response. Additional exploratory objectives include evaluation of changes in biomarkers in blood and tissue samples collected from patients that may reflect entinostat activity on immune cells.

Details of the trial design are provided below:



Entinostat with Immune Checkpoint Inhibitors in TNBC

Market Overview and Current Treatment

Breast cancer is the leading cause of cancer death in women worldwide and the second leading cause of cancer death in women in the United States after lung cancer. According to the American Cancer Society, in 2017 approximately 253,000 new cases of invasive breast cancer will be diagnosed in the United States and an estimated 41,000 people will die from breast cancer in the United States. Although the five-year survival rate for women diagnosed with non-metastatic breast cancer is over 85%, the five-year survival rate for women diagnosed with metastatic breast cancer is only 24%, indicating the need for new therapies that can prolong overall survival.

Breast cancers can be divided into three subsets based on the presence or absence in the tumor of the following protein receptors:

- HR+, which means expressing the estrogen receptor, or ER, or progesterone receptor, or PR, alone or in combination with each other;
- HER2+, which means expressing the human epidermal growth factor receptor 2, or HER2 receptor; and
- Triple negative, which means not expressing ER, PR or HER2.

TNBC represents 15-20% of newly diagnosed breast cancer cases, and is associated with a younger age at diagnosis, advanced stage at diagnosis, increased risk of visceral metastasis and poorer outcome. The five-year survival rate for women diagnosed with Stage IV TNBC is only 22% with limited treatment options. Preliminary data has indicated that treatment with PD-L1 inhibitors results in approximately a 20% response rate in women with TNBC, and Tecentriq and Keytruda are currently being studied in Phase 3 clinical trials.

Our Development Plan of Entinostat in TNBC

We established a clinical collaboration with Genentech to study the safety and efficacy of entinostat in combination with atezolizumab, an anti-PD-L1 antibody, in patients with TNBC. The ENCORE 602 clinical trial

is a Phase 1b/2 clinical trial, and the Phase 1b portion is initially evaluating the safety of weekly oral entinostat at a dose of 5 mg administered in combination with 1,200 mg of atezolizumab given intravenously every three weeks. Enrollment in the Phase 1b trial was completed in November 2016. The RP2D of entinostat was established as 5 mg weekly. The Phase 2 portion of the trial was opened in December 2016. The Phase 2 portion of the clinical trial is a randomized, double-blind, placebo-controlled trial. The primary endpoint of the Phase 2 clinical trial is PFS, with response rate, duration of response, time to response and overall survival as secondary end points. Additional exploratory objectives include evaluation of changes in biomarkers in blood and tissue samples collected from patients that may reflect entinostat activity on immune cells. We anticipate efficacy and safety data from the Phase 2 portion in 2018.

Entinostat with Immune Checkpoint Inhibitors in Ovarian Cancer

Market Overview and Current Treatment—Ovarian Cancer

The American Cancer Society indicates that approximately 22,000 women will be diagnosed and just over 14,000 will die from ovarian cancer in the United States in 2017. The past few decades have seen some improvement in median five-year survival for women diagnosed with ovarian cancer, but the trend has been modest, increasing from 36% in 1977 to 45% in 2017.

Currently, more than 60% of women are diagnosed with advanced disease and therapeutic options for these patients are still dominated by traditional chemotherapeutics, such as platinums, taxanes and anthracyclines. Since 2014, three targeted agents have been approved for later line treatment of refractory patients: *Avastin*® (bevacizumab), a vascular endothelial growth factor specific angiogenesis inhibitor, and two poly ADP-ribose polymerase, or PARP, inhibitors, *Lynparza*® (olaparib), and *Rubraca*™ (rucaparib), which recently received accelerated approval for patients with deleterious breast cancer susceptibility gene, or BRAC, mutations. However, the median duration of response to any of these drugs was still less than 10 months, highlighting the need to further improve upon patient care. The safety and the efficacy of immune-targeted therapy in ovarian cancer has not yet been demonstrated, but *Tecentriq* and avelumab are in Phase 3 development.

Our Development Plan of Entinostat in Ovarian Cancer

We have a clinical trial collaboration with Merck KGaA and Pfizer to study the safety and efficacy of entinostat in combination with avelumab, an investigational anti-PD-L1 antibody, in patients with ovarian cancer. The ENCORE 603 clinical trial is designed as a Phase 1b/2 clinical trial, where the Phase 1b portion will initially evaluate the safety of weekly, oral entinostat with avelumab. If this combination is well tolerated, the Phase 2 portion of the clinical trial will be designed as a randomized, double-blind, placebo-controlled trial. The primary endpoint of the Phase 2 clinical trial will be PFS, with response rate, duration of response, time to response and overall survival as secondary end points. Additional exploratory objectives include evaluation of changes in biomarkers in blood and tissue samples collected from patients that may reflect the effect of entinostat on immune cells. Enrollment of patients into the Phase 1b portion of the ENCORE 603 clinical trial began in January 2017; and safety data, including the determination of the RP2D, is expected from the Phase 1b portion in the first half of 2017.

Investigator-Sponsored Clinical Trials of Entinostat in Immuno-Oncology

We believe that there are additional opportunities for expanding the indications in which entinostat may target immunologic mechanisms of resistance to cancer therapies. In addition to our collaborations with Merck, Genentech, Merck KGaA and Pfizer, we have partnered with independent investigators to support clinical trials that are designed to validate both clinical and preclinical observations that entinostat can enhance the clinical activity of immune therapy in patients. We do not control the timing of these clinical trials and cannot provide any assurance with respect thereto.

J1353: Epigenetic Priming to Immunotherapy Trial. This JHU investigator-sponsored Phase 2 clinical trial, funded by *Stand Up To Cancer*, is currently enrolling up to 90 patients with metastatic NSCLC and is designed to test the ability of epigenetic therapy—a combination of entinostat and *Vidaza*—to enhance the response of NSCLC patients to *Opdivo*.

NCI-7870: Entinostat + High Dose Interleukin in Metastatic Renal Cell Carcinoma. This investigator-sponsored Phase 1/2 clinical trial funded by the NCI was designed to determine the safety and efficacy of entinostat combined with *Proleukin*, an approved immune therapy for patients with metastatic renal cell carcinoma. *Proleukin* as a single agent in metastatic renal cell carcinoma has demonstrated a 15% to 25% objective response rate and approximately four months median PFS. The clinical trial was designed to test whether entinostat combined with *Proleukin* could increase the primary endpoint of response rate from 20% to 40%; the secondary endpoint was PFS. Entinostat was dosed orally starting at 3 mg once every other week, and once that dose was shown to be well-tolerated, additional patients were enrolled at a dose of 5 mg of entinostat once every other week. *Proleukin* was provided at the standard dose of 600,000 units/kg every eight hours for five days followed by a second course. Preliminary results from the completed Phase 1 portion indicated that entinostat may be given safely in combination with *Proleukin* and indicated that entinostat potentially enhances the response to *Proleukin* with evidence of causing beneficial changes in certain immune cell functions such as reduction of immune-suppressive Tregs. Phase 1 portion indicated that entinostat can be given safely in combination with *Proleukin* and indicated that entinostat potentially enhances the response to *Proleukin* with evidence of causing beneficial changes in certain immune cell functions such as reduction of immune-suppressive Tregs. The Phase 2 portion of the trial has completed enrollment with 47 patients evaluable for safety and 43 evaluable for efficacy. Data were presented at the annual meeting of the American Society of Clinical Oncology in June 2016 demonstrating a response rate of 37% (95% CI 22, 53%) in 41 patients with measurable disease and a median PFS of 13.8 months (95% CI 6.0, 18.8 months). The investigators concluded that the results suggest that entinostat may increase the anti-tumor activity of *Proleukin* by modulating immunosuppressive cells.

NCI-9844: Efficacy of Entinostat in Combination with *Opdivo* and *Yervoy* in Patients with Metastatic or Unresectable Solid Tumors. This investigator-sponsored Phase 1 clinical trial, which is being sponsored by the NCI, is designed to enroll up to 39 patients to study the safety profile and best dose of entinostat and *Opdivo* when given together with *Yervoy* in treating patients with metastatic or unresectable solid tumors or metastatic HER2- breast cancer. The trial began enrolling patients in the first quarter of 2016 with data expected in the second half of 2017.

Entinostat in Advanced HR+ Breast Cancer

Market Overview and Current Treatment

In the past, certain patients in the United States with advanced HR+ breast cancer were treated with hormone therapies with the goal to prolong overall survival 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 overall survival. Resistance to hormone therapies develops as a result of activation of growth-factor signaling pathways. The median overall survival for advanced HR+ breast cancer in the first- and second-line setting is approximately three to four years and two years, respectively.

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. Researchers have demonstrated that the diminished clinical benefit of each hormone therapy is due to primary and acquired resistance to hormone therapy. The cause of resistance is multi-factorial and results in tumor progression independent of estrogen stimulation.

Current treatment of advanced HR+ breast cancer usually includes multiple courses of hormone therapy followed ultimately by chemotherapy. There are three types of commonly used hormone therapies. These are

Soltamox® (tamoxifen), a selective ER modulator, *Faslodex*® (fulvestrant), a selective ER downregulator, and aromatase inhibitors, such as *Arimidex*® (anastrozole), *Femara*® (letrozole) and *Aromasin*, which interfere with estrogen production. *Aromasin*, a steroidal aromatase inhibitor, is typically used as a second- or third-line treatment upon progression from first-line treatment with the non-steroidal aromatase inhibitors *Arimidex* and *Femara*.

In 2012, the FDA approved *Afinitor*® (everolimus), an inhibitor of mammalian target of rapamycin for the treatment of postmenopausal women with advanced HR+ and HER2-, breast cancer in combination with *Aromasin*, after failure of treatment with *Femara* or *Arimidex*. The approval was based on results from a randomized Phase 3 clinical trial of postmenopausal women with advanced estrogen receptor-positive, HER2-, breast cancer with recurrence or progression following prior therapy with *Femara* or anastrozole. The median PFS was 7.8 months for patients receiving *Afinitor* and 3.2 months for patients receiving placebo. Based on these results, *Afinitor* has become a treatment option for patients refractory to aromatase inhibitor therapy. However, the combination of *Aromasin* and *Afinitor* did not confer an improvement in overall survival.

More recently, in early 2015, the FDA granted accelerated approval to *Ibrance*® (palbociclib), a cyclin-dependent kinase 4 and 6 inhibitor, or CDK4/6, for the treatment of breast cancer in the first-line setting in postmenopausal women with metastatic disease, in combination with *Femara*, an aromatase inhibitor. The approval of *Ibrance* was based on the results of a randomized Phase 2 clinical trial of postmenopausal women with ER+, HER2- breast cancer, which demonstrated a 10-month increase in median PFS for the combination of *Ibrance* and *Femara* versus *Femara* alone. During the first quarter of 2016, the FDA granted approval to *Ibrance* for use in combination with *Faslodex* in women with HR+, HER2- breast cancer disease progression following endocrine therapy. Overall survival has not been reported for *Ibrance* clinical trials to date. However, based on the significant PFS benefit observed with *Ibrance* with endocrine therapy, it has become the standard first-line therapy in this patient population.

Ribociclib, a CDK4/6 inhibitor from Novartis International AG, or Novartis, has demonstrated PFS benefit in a Phase 3 trial in combination with letrozole. Novartis has indicated that it expects an approval decision for *ribociclib* from the FDA in the first half of 2017. Based on the results and preclinical cross resistance between *Ibrance* and *ribociclib*, we believe *ribociclib*, if approved, would compete for the patient population already being treated by *Ibrance*.

While the treatment of advanced HR+ breast cancer is evolving given the introduction of both *Ibrance* and *Afinitor*, we believe physicians will welcome the introduction of a well-tolerated therapy that improves overall survival, which has not been demonstrated to date for either *Ibrance* or *Afinitor* in combination with hormone therapy. Current data suggest that entinostat could demonstrate a favorable benefit-risk profile and an improvement in overall survival, 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.

Our Development of Entinostat in Advanced HR+ Breast Cancer

We have completed a Phase 2b clinical trial, ENCORE 301, of entinostat in advanced HR+ breast cancer in 130 postmenopausal patients. The trial was a randomized, placebo-controlled clinical trial in which treatment with entinostat was observed to result in a significant advantage to patients when given in addition to *Aromasin* therapy. Postmenopausal patients with advanced HR+ breast cancer progressing on a non-steroidal aromatase inhibitor were randomly assigned to the combination of *Aromasin* (25 mg daily) and entinostat (5 mg once per week) or to the combination of *Aromasin* (25 mg daily) and a placebo. The primary endpoint was PFS, with overall survival as an exploratory endpoint.

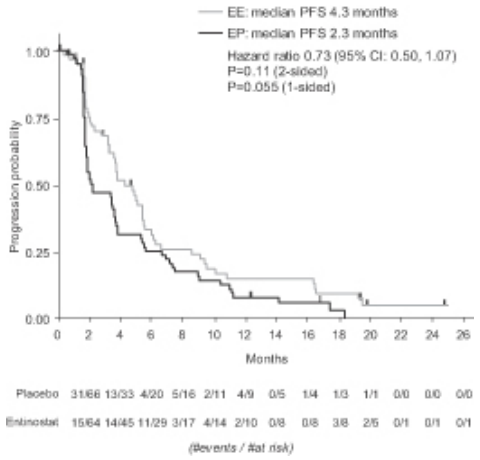
A Kaplan-Meier plot is a graphical statistical method commonly used to describe survival characteristics. The following are explanations of the meanings of the various efficacy endpoints that we have used in describing

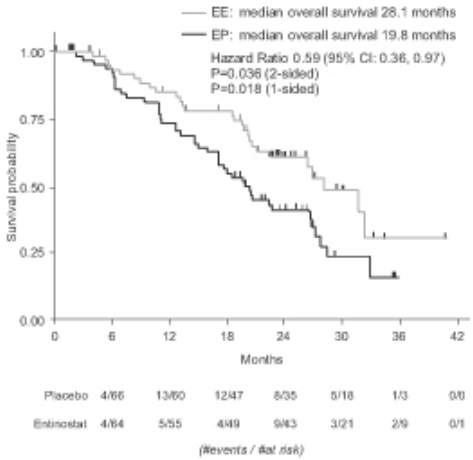
the results of our Phase 2b clinical trial. Each is determined in accordance with Response Criteria in Solid Tumors measurement guidelines.

- **P-value**: a statistical measure that represents the probability that the difference that is observed between two treatment arms is due to random chance and is not actually related to the treatments being compared. For example, p-value of 0.1 indicates there is a 10% chance the difference that is observed between the treatment arms is due to random chance.
- **Confidence interval**: a statistical measure that indicates a range, which is believed to include the true effect parameter with some level of confidence. For example, a 95% CI is the range at which one is 95% sure, with a 5% chance of being wrong, that the range given includes the true effect parameter.
- **Hazard ratio**: represents the chance of events occurring in the treatment arm relative to the chance of events occurring in the control arm. A hazard ratio of one means that there is no difference in survival between the two groups. A hazard ratio of greater than one or less than one means that survival was better in one of the groups.

The trial met the statistical criteria for a positive PFS endpoint using a pre-specified p-value of 0.10 from a one-sided test for statistical significance. The overall survival benefit observed in the entinostat/*Aromasin* (exemestane tablets) (EE) group was also statistically significant versus the *Aromasin* (exemestane tablets)/placebo (EP) group. The results are summarized below along with the Kaplan-Meier plot for PFS and overall survival.

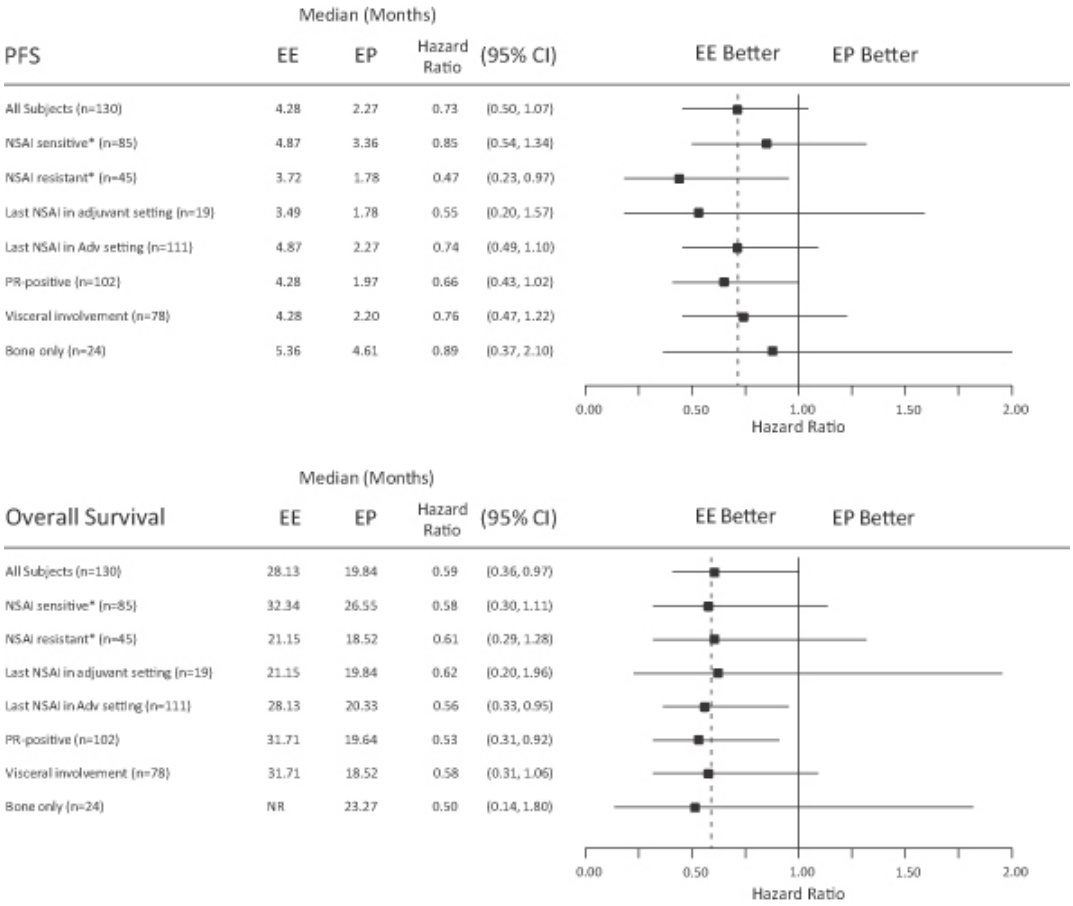
- Median PFS approximately doubled to 4.3 months in the EE group versus 2.3 months in the EP group, corresponding to a statistically significant hazard ratio of 0.73; 95% CI, 0.50 to 1.07; P2-sided=0.11; P1-sided=0.055.
- Median overall survival improved to 28.1 months in the EE group versus 19.8 months in the EP group, corresponding to a statistically significant hazard ratio of 0.59; 95% CI, 0.36 to 0.97; P2-sided=0.036; P1-sided=0.018.
- Fatigue and neutropenia were the most frequent Grade 3 and Grade 4 toxicities.





We have utilized forest plots, which are a form of graphical display designed to illustrate the relative strength of treatment effects across multiple subgroups, to highlight the consistency of the clinical benefit of EE treatment across multiple subgroups for both the PFS and overall survival endpoints. In addition, we analyzed the post-study treatments that patients received to determine whether there were imbalances in the subsequent treatment that could account for the difference in overall survival observed between the EE and EP groups. The

two groups were well balanced for the first and all subsequent cancer therapies, which suggest that a favorable result for overall survival is unlikely due to differences in the therapies patients received after discontinuing study treatment.



Plot Legend

- NSAI: non-steroidal aromatase inhibitor.
- Visceral involvement: refers to advanced HR+ breast cancer that has spread to any of the internal organs in the body.
- NSAI sensitive: indicates a complete response, partial response or stable disease greater than six months on prior non-steroidal aromatase inhibitor therapy; all other patients considered NSAI resistant.

Safety was assessed by utilizing the NCI's Common Terminology Criteria for Adverse Events—Version 3. When entinostat was added to *Aromasin*, the adverse event, or AE, profile was consistent with previous clinical experience with entinostat treatment. Overall, the EE group had a higher rate of AEs versus the EP group at 95% and 85%, respectively, with the most common AEs in the EE group being fatigue, gastrointestinal disturbances, such as nausea, vomiting and diarrhea, and hematologic toxicities, such as uncomplicated neutropenia, thrombocytopenia and anemia. The EE group had more AEs leading to dose modification (35% versus 6%), and more AEs leading to study discontinuation (11% versus 2%), irrespective of study drug relationship.

For hematological toxicities, thrombocytopenia was managed by dose modification during entinostat treatment, with all cases being non-severe and none requiring drug discontinuation. In approximately half of the patients who experienced Grade 3 neutropenia, it was managed by dose modification, with only one case leading to entinostat discontinuation. Additional reasons leading to EE discontinuation included two patients owing to nausea and vomiting and one patient each owing to weakness in extremities, hypoxia/radiation pneumonitis, fatigue and mucositis.

The incidence of serious AEs was similar between the EE and EP groups at 16% and 12%, respectively, with four EE patients each experiencing a Grade 4 AE, including fatigue, leucopenia, neutropenia and hypercalcemia. One fatal AE occurred in each treatment arm with the EE event considered related to disease progression. We did not observe significant cardiovascular effects in this trial, which have been reported with other HDAC inhibitors.

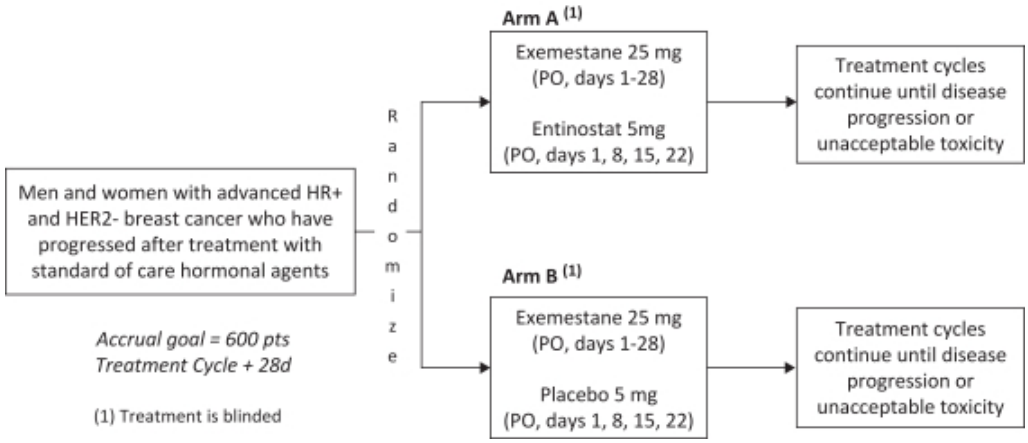
Following positive results from our Phase 2b clinical trial, entinostat in combination with *Aromasin* was granted breakthrough therapy designation by the FDA in advanced HR+ breast cancer and is currently being evaluated in a Phase 3 clinical trial for advanced HR+, HER2- breast cancer.

E2112: Ongoing Pivotal Phase 3 Clinical Trial

In order to confirm the PFS and overall survival benefits observed in the Phase 2b clinical trial, we have partnered with ECOG-ACRIN to develop and conduct the Phase 3 clinical trial. 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 *Aromasin* compared to *Aromasin* 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. The trial initiated enrollment of 600 patients in the second quarter of 2014. Based on information received from ECOG-ACRIN to date, we expect that the trial will require at least 40 months to fully enroll patients with primary PFS endpoint data expected no sooner than the end of the second half of 2017. Since we are not responsible for the conduct of the E2112 clinical trial, we cannot provide assurance that this trial will be completed or that data will be received on the timeline indicated.

The primary objective of the trial is to evaluate whether the addition of entinostat to *Aromasin* improves PFS, overall survival or both PFS and overall survival 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*. The NCI and ECOG-ACRIN, in collaboration with us, have designed the trial to have two primary endpoints of PFS and overall survival. If data are positive, we expect that either endpoint may serve as the basis for submitting a new drug application, or NDA. The Phase 3 clinical trial also contains secondary patient-reported outcomes, or PRO, endpoints to evaluate differences between arms in treatment toxicities, reduced symptom burden as an indicator of treatment response, and overall health-related quality of life. PRO measures are common in ECOG-ACRIN therapeutic trials due to the scientific aims of its Cancer Control & Outcomes Program, which seeks to increase understanding, from the patient perspective, about how novel therapies impact quality of life. Secondary objectives of the trial include assessments of safety, response rate and biomarker analysis.

Details of the trial design are provided below:



The enrollment size of 600 patients in the trial is adequate for achieving a statistically significant difference in median PFS with a p-value less than 0.002 and in median overall survival with a p-value less than 0.048 based on the trial supporting a hypothesized hazard ratio of 0.58 for PFS and 0.75 for overall survival. If the hypothesized hazard ratio for PFS is true, the PFS endpoint has an 88.5% chance of success. Similarly, if the hypothesized hazard ratio of overall survival is true, the overall survival endpoint has an 80% chance of success.

The primary analysis of PFS will be conducted when 247 PFS events occur out of the initial 360 patients enrolled. At the time of the primary PFS analysis, the first interim analysis of overall survival will also be conducted. Stopping rules based upon the interim analyses of overall survival have been outlined such that enrollment may terminate early if the statistical boundary for overall survival is met. Because of the smaller numbers of patients and limited length of follow-up at the time of the first interim analysis of overall survival, we do not expect to meet the criteria for early stopping at that time.

In the absence of early stopping, the results of the primary analysis of PFS will be made available to us when all 600 patients have entered the trial, which is anticipated to be no sooner than the second half of 2017. If the PFS endpoint is met, interim overall survival results will be released to us at that time as well. If the overall survival data demonstrate a positive trend, we expect they will be used to supplement new drug application, or NDA, submission based on meeting the primary PFS endpoint and agreement with the FDA that the PFS data are statistically significant and clinically meaningful to support an NDA submission.

The primary analysis of overall survival data represents another opportunity for submission of an NDA to the FDA for potential approval. The primary analysis of overall survival will occur when 410 deaths from among the 600 patients enrolled have occurred. Based on information received from ECOG-ACRIN to date, we expect this analysis to occur no sooner than 2019.

In addition to these analyses, if the primary analysis of PFS fails to achieve statistical significance, a positive overall survival outcome at any interim analysis during the conduct of the trial will also be a potential approval pathway. ECOG-ACRIN will perform up to seven interim analyses of overall survival, approximately every six months, to assess the potential superiority of the combination of entinostat and *Aromasin* relative to the combination of *Aromasin* and a placebo. The 410 deaths required for the primary analysis of overall survival takes into consideration any statistical impact of the various interim analyses on the analysis of the overall survival endpoint. If the interim analyses do not demonstrate a statistically significant overall survival benefit, ECOG-ACRIN will not release the results of such interim analyses to us.

Additional Clinical Trials in Support of the Entinostat NDA Entinostat

In parallel with the pivotal Phase 3 clinical trial, we are conducting a number of required clinical pharmacology trials required for the submission of the NDA for entinostat. In 2015, we conducted a Phase 1 clinical trial to determine how much entinostat is absorbed by patients, how it is distributed in the body and how it is metabolized and excreted. Results of this clinical trial were released in 2016 and consistent with prior entinostat pharmacokinetic data and showed that entinostat is primarily excreted through the kidneys. Data results have also lead to an investigation into whether or not identification of other entinostat metabolites are necessary.

We are currently conducting a Phase 1 clinical trial, which was initiated in June 2016, to determine whether entinostat interferes with the pharmacological properties of *Aromasin* (drug-drug interaction trial) and a Phase 1 clinical trial, which was initiated in September 2016, to confirm previous findings that there are no cardiac safety signals associated with entinostat treatment. Other trials, which were initiated in the second half of 2016 include a healthy volunteer trial of the effect of proton pump inhibitors on entinostat and a healthy volunteer trial to examine the pharmacokinetics of the effects of food on entinostat dosing. These trials are expected to have data readouts in the second half of 2017.

We also anticipate conducting a drug-drug interaction trial to determine whether entinostat interferes with the pharmacological properties of midazolam in healthy volunteers. A clinical trial to assess whether or not patients with renal impairment are able to achieve clearance of entinostat to the same extent as patients without renal impairment, is also planned in 2017 with data expected by the end of 2017.

Additional Development Activities of Entinostat

We are currently collaborating with the NCI and investigators on combination trials of entinostat with other therapies across additional multiple tumor types such as HER2+ breast cancer, NSCLC and acute myeloid leukemia. Each of these trials is being funded either by the NCI or as investigator-initiated studies funded through grants and sponsoring institutions. Since we are not responsible for the conduct of these clinical trials, we cannot provide assurance that they will be completed or that data will be received on the timeline indicated.

- **NCI-8871: HER2+ Breast Cancer.** We are collaborating with investigators at MD Anderson Cancer Center to determine whether the addition of entinostat to a second HER2 targeted therapy can overcome the resistance that had developed in response to prior HER2 targeted therapy. A Phase 1 dose escalation trial of entinostat with *Tykerb*® (lapatinib), a small molecule dual inhibitor of HER2 and EGFR signaling, has established the feasibility and safety of that combination. A second Phase 1 clinical trial studying entinostat in combination with *Tykerb* and *Herceptin*® (trastuzumab), a monoclonal antibody inhibitor of HER2 signaling, has recently completed patient enrollment and has established the feasibility and safety of the triple combination. A total of 37 patients have been enrolled in the Phase 1 trial. Preliminary data from this trial was presented at the 2015 San Antonio Breast Cancer Symposium with the authors concluding that entinostat combined with *Tykerb* and *Herceptin* was generally well tolerated with preliminary evidence of efficacy in metastatic HER2+ patients whose disease progressed on *Herceptin*.
- **NCI-9253: Epigenetic Priming to Chemotherapy.** This NCI-sponsored Phase 2 clinical trial is currently enrolling up to 165 patients with advanced NSCLC and is designed to test the ability of epigenetic therapy—a combination of entinostat and *Vidaza*—to enhance the response of NSCLC patients to chemotherapy. Data from this trial are expected in the second half of 2017.

SNDX-6352

We and our collaborators 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. UCB Biopharma Sprl, or UCB, has demonstrated in preclinical studies that were designed to measure the amount of SNDX-6352 bound to the CSF-1R, that SNDX-6352 binds

to human CSF-1R with high affinity as indicated by a dissociation constant value, or KD, of 4-8 picomolar (pM). These studies also showed that SNDX-6352 can bind to human and cynomolgus monkey CSF-1R but not rodent CSF-1R.

One way in which investigators show that CSF-1 and IL-34 bind to and activate CSF-1R is to measure the amount of a secreted factor known as monocyte chemotactic protein 1, or MCP-1, that is released by cells when CSF-1R signaling is activated. A lower amount of MCP-1 can mean that the binding of CSF-1 and IL-34 have been blocked. Preliminary research shows that SNDX-6352 potently inhibits both CSF-1 and IL-34 induced MCP-1 release from human monocytes (IC50, 270pM and 100pM, respectively).

A second way in which investigators measure the activity of CSF-1R blockade is to count the number of circulating cells known as non-classical monocytes. The cells can be identified by expression of cell surface markers called CD14 and CD16. Researchers have shown that blocking CSF-1R signaling results in a decrease in the number of non-classical monocytes, and SNDX-6352 has been shown to reduce the number of non-classical monocytes in a preclinical trial.

A third way to demonstrate that SNDX-6352 can bind to CSF-1R and block binding of CSF-1 is to measure the level of circulating CSF-1 in the blood. Researchers have shown that blocking CSF-1R results in increased levels of CSF-1. The amount of circulating CSF-1 can therefore be used as measurement of the amount of SNDX-6352 bound to CSF-1R. In order to understand the expected clinical activity of SNDX-6352 in human subjects, we and our collaborators have conducted studies with SNDX-6352 across a range of doses in cynomolgus monkeys. Our preclinical data indicate that SNDX-6352 causes sustained increases in CSF-1 levels for at least 14 days at doses greater than 5 mg per kilogram of bodyweight.

We believe that the results of UCB's preclinical studies combined demonstrate that SNDX-6352 is a potent CSF-1R binding antibody that can block the activation of CSF-1R signaling through both IL-34 and CSF-1 and reduce the number of CSF-1R expressing target cells.

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) and where we believe that the inhibition of TAMs via CSF-1R inhibition will synergize with the current standard of care, inducing tumor regressions.

In order to determine the initial safety profile of SNDX-6352, we commenced SNDX-6352-0001, a single ascending dose Phase 1 clinical trial in the fourth quarter of 2016. In addition to assessing safety assessment at increasing doses of SNDX-6352, we will collect 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 in the Netherlands and will be enrolling up to 36 healthy subjects. We expect to complete enrollment in this Phase 1 trial by the end of second quarter of 2017. We expect to utilize the safety assessment of single doses of SNDX-6352 in deciding the starting dose for subsequent clinical trials testing multiple doses of SNDX-6352 as a single agent and in combinations.

Collaborations

Clinical Collaborations in Immuno-Oncology

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 will supply *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.

To the extent any inventions arise from the clinical trial, 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. However, each party will separately analyze clinical samples obtained from trial participants, and each party will solely own the sample analysis data that it generates.

Either party may terminate the agreement for the other party's uncured material breach. In addition, either party may terminate the agreement if it believes that there is imminent danger to patients in the clinical trial, or if a regulatory authority takes an action that prevent such party from supplying its drug, or if such party decides to discontinue development of its drug. Merck may terminate the agreement if we fail to make any changes to the clinical trial protocol that are reasonably requested by Merck to address a perceived safety issue or if we undergo a change of control with a company that is clinically developing or marketing a drug having the same mechanism of action as *Keytruda*.

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 atezolizumab in patients with TNBC. We will be the sponsor of the clinical trial. Genentech will supply atezolizumab for use in the clinical trial. Each party will perform its obligations under the agreement at its own expense, including its internal costs.

To the extent any inventions arise from the clinical trial, 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, data from the trial will be jointly owned. However, each party will solely own certain sample analysis data generated from clinical samples obtained from trial participants.

Either party may terminate the agreement for the other party's uncured material breach. In addition, either party may terminate the agreement if it determines that the trial may unreasonably affect patient safety, or if a regulatory authority withdraws the approval to conduct the 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 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, avelumab, in patients with ovarian cancer. Avelumab is being developed collaboratively by Merck KGaA and Pfizer, which are together treated as a single party for purposes of this agreement. We will be the sponsor of the clinical trial. Merck KGaA and Pfizer will supply avelumab for use in the clinical trial. During the term of the trial or the term of the agreement, whichever is shorter, each party has agreed not to initiate any clinical trial in combination with such party's drug and a third party drug for the treatment of ovarian cancer if the third party drug has the same target and mechanism of action as the other party's drug, subject to certain exceptions.

To the extent any inventions arise from the clinical trial, 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, data from the trial will be jointly owned. However, each party will solely own certain sample analysis data generated from clinical samples obtained from trial participants.

Either party may terminate the agreement for the other party's uncured material breach. In addition, either party may terminate the agreement if it determines that the trial may unreasonably affect patient safety, or if a regulatory authority takes an action that prevent such party from supplying its drug, or if such party decides to discontinue development of its drug. Merck KGaA and Pfizer may also terminate the agreement if we fail to make any changes to the clinical trial protocol that are reasonably requested by them to address a perceived safety issue.

NCI and Investigator Collaborations

Collaborative Research and Development Agreement with the NCI related to Entinostat

Our collaboration with the NCI is governed by a cooperative research and development agreement, or 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, 2017. 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 will perform 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 $695,000 and a series of time- and milestone-based payments of up to $970,000, and we are obligated to supply entinostat and placebo to ECOG-ACRIN for use in the clinical trial. During the second quarter of 2016, the agreement was amended to provide additional study activities and the contractual obligation increased by $0.8 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, 2016, our aggregate payment obligations under this agreement are approximately $21.4 million; and our remaining obligations under this agreement were $12.9 million over an estimated period of approximately four years. During the first quarter of 2017, the agreement was amended to expand the study to include enrollments from Korean sites, and the contractual obligation increased by $0.5 million.

Data and inventions from the Phase 3 clinical trial are owned by ECOG-ACRIN. 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 in the course of 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.

Investigator Collaborations

We have collaborated with a limited number of third parties on the clinical development of entinostat and SNDX-6352. For example, we have supplied entinostat for use in investigator-sponsored clinical trials conducted at JHU and we plan to enter into similar arrangements with other hospitals and medical centers in the future. Investigator-sponsored clinical trials are generally performed under an IND application filed by the investigator or his or her institution. To date, our sole obligation with respect to these investigator-sponsored clinical trials has been to supply entinostat for use in the trials.

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 1 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 1 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. 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 build a commercial infrastructure to support sales of entinostat and SNDX-6352 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 or SNDX-6352, 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 or SNDX-6352 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.

Competition

The pharmacologic treatment of NSCLC, melanoma, ovarian cancer and TNBC patients includes chemotherapies and therapies targeting specific gene mutations. More recently, immune checkpoint inhibitors have been approved for NSCLC and melanoma and are under investigation for ovarian cancer and TNBC. In October 2015, the FDA approved for the first time the combination of two immuno-oncology drugs, *Opdivo* and *Yervoy*, for the treatment of melanoma. There are currently numerous drugs undergoing active clinical investigation. We believe that if entinostat in combination with *Keytruda*, atezolizumab or avelumab were

approved for the treatment of NSCLC, melanoma, TNBC or ovarian cancer, it would face competition from these standard-of-care approaches and other investigational drugs being tested in combination with any of these approaches.

If entinostat in combination with *Aromasin* 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* developed by Pfizer, *Afinitor* developed by Novartis, and other therapies currently in Phase 3 clinical development such as abemaciclib being developed by Eli Lilly and Company, and ribociclib and buparlisib both of which are being developed by Novartis.

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 we may be 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 expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price and the availability of reimbursement from government and other third-party payors.

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 entinostat and SNDX-6352, its methods of use and processes for its 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, 2016, our portfolio included two owned U.S. provisional patent applications, two owned pending U.S. non-provisional patent applications one granted non-U.S. patent and 19 non-U.S. pending patent applications (including four 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

Aromasin. 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 *Aromasin* 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. 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 and methods of treating lung cancer patients by administration of entinostat in combination with an EGFR inhibitor. Our owned pending U.S. provisional and PCT applications relate to treatments with entinostat combined with anti PD-1 or anti PD-L1 antibodies. If issued, patents based on our owned pending U.S. applications and non-U.S. filings based on our owned PCT application would expire between April 2029 and December 2036.

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, 2016, 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 expiring 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 expires 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 expires in October 2017, covers methods of treating selected cancers by administration of entinostat; U.S. Patent 7,687,525, which also expires 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 expires 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 expires in September 2017, covers a subgenus of benzamide compounds that does not include entinostat; and U.S. Patent 6,794,392, which expires 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 patent portfolio directed to SNDX-6352, an IND-ready anti-CSF-1R monoclonal antibody. As of December 31, 2016, the SNDX-6352 composition-of-matter patent portfolio included one pending U.S. non-provisional patent application, one granted non-U.S. patent and 38 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 2024.

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 were obligated to pay 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. In June 2014, we achieved a research and development milestone, and in accordance with the terms of the Bayer license agreement, we paid $2.0 million to Bayer.

We are also obligated to pay Bayer $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.

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 under the Federal Food, Drug, and Cosmetic Act, or FDCA, and related regulations. Drugs 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.

The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of any product candidates, product or manufacturing changes, additional disease indications, or label changes. We cannot predict the likelihood, nature or extent of government regulation that might arise from future legislative or administrative action.

Failure to comply with the applicable United States regulatory requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial enforcement actions. These actions could include the suspension or termination of clinical trials by the FDA, the FDA's refusal to approve pending applications or supplemental applications, withdrawal of an approval, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, import detention, injunctions, fines, civil penalties or criminal prosecution. Any such administrative or judicial action could have a material adverse effect on us.

Although this discussion focuses on regulation in the United States, we anticipate seeking approval for and marketing of our product candidates in other countries. Generally, our product candidates will be subject to regulation in other countries that is similar in nature and scope as those imposed in the United States, although there can be important differences. In Europe, for example, some significant aspects of regulation are addressed in a centralized way through the European Medicines Agency, but country-specific regulation remains essential in many respects.

Drug Development Process

The process required by the FDA before drugs 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;
- a determination by the FDA within 60 days of its receipt of an NDA to accept an NDA for filing and review;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the drug 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 drug'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; and
- FDA review and approval of an NDA prior to any commercial marketing or sale of the drug in the United States.

Preclinical Testing

Before testing any compounds with potential therapeutic value in humans, the drug 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 drug candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs.

IND Application

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.

Clinical Trials

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. 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.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and written IND safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events or any finding from tests in laboratory animals that suggests a significant risk for human subjects. Phase 1, Phase 2 and Phase 3 clinical trials may fail to be completed successfully within any specified period, if at all. The FDA, the IRB or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, 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 drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and, among other things, must include developed methods for testing the identity, strength, quality and purity of the finished drug product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf life.

FDA Review and Approval Processes

In order to obtain approval to market a drug 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 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 for completeness before it accepts it for filing. The FDA has 60 days from its receipt of an NDA 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 an NDA 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 submission is accepted for filing, the FDA reviews an NDA 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, 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. Whether priority or standard review applies, an additional 60 days is added to the target date for FDA action for new molecular entities.

After the FDA completes its initial review of an NDA, it will communicate to the sponsor that the drug will either be approved, or it will issue a complete response letter to communicate that an NDA 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, with no implication regarding the ultimate approvability of the application.

Before approving an NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical sites to assure compliance with GCP. If the FDA determines the application, manufacturing process or manufacturing facilities are not acceptable, it typically will outline the deficiencies and often will request additional testing or information. This may significantly delay further review of the application. If the FDA finds that a clinical site did not conduct the clinical trial in accordance with GCP, the FDA may determine the data generated by the clinical site should be excluded from the primary efficacy analyses provided in an NDA. Additionally, notwithstanding the submission of any requested additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

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. Depending on the FDA's evaluation of a drug's risks, a REMS may include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution requirements, patient registries and other risk minimization tools. Following approval of an NDA with a REMS, the sponsor is responsible for marketing the drug in compliance with the REMS and must submit periodic REMS assessments to the FDA.

Further, even after regulatory approval is obtained, later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. In addition, we cannot predict what adverse governmental regulations may arise from future U.S. or foreign governmental action.

Expedited Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. For a Fast Track product, the FDA may consider for review sections of an NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of an NDA, the FDA agrees to accept sections of an NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of an NDA.

Any product submitted to the FDA for approval, including a product with a Fast Track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. Drug products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug product receiving accelerated approval perform adequate and well-controlled post-marketing clinical studies. In addition, the FDA requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

The FDA may also expedite the review of a drug designated as a breakthrough therapy, which is a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. 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. The designation of a drug as a breakthrough therapy provides the same benefits as are available under the Fast Track program, as well as intensive FDA guidance on the product's development program. 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.

Fast Track designation, priority review, accelerated approval and Breakthrough Therapy designation do not change the standards for approval, but may expedite the development or review process.

Hatch-Waxman Act

Under the Drug Price Competition and Patent Term Restoration Act of 1984, known as the "Hatch-Waxman Act," Congress created an abbreviated FDA review process for generic versions of approved pioneer (brand name) NDA products. In considering whether to approve such a generic drug product submitted under an Abbreviated New Drug Application, or ANDA, the FDA generally requires that an ANDA applicant demonstrate that the proposed generic drug product's active ingredient, strength, dosage form, and route of administration are the same as that of the reference product, that the two drugs are bioequivalent, that any impurities in the proposed product do not affect the product's safety or effectiveness, and that its manufacturing processes and methods ensure the consistent potency and purity of its proposed product. Similarly, section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act provides a reduced burden of demonstrating safety and effectiveness for an NDA for a product that is similar, but not identical, to the pioneer product.

The Hatch Waxman Act requires NDA applicants and NDA holders to provide certain information about patents related to the drug for listing in its publication Approved Drug Products with Therapeutic Equivalence Evaluations, referred to as the Orange Book. ANDA and 505(b)(2) applicants who seek to reference a pioneer drug must then certify regarding each of the patents listed with the FDA for the reference product. A certification that a listed patent is invalid or will not be infringed by the marketing of the applicant's product is called a "Paragraph IV certification."

The Hatch Waxman Act also provides periods of regulatory exclusivity for certain pioneer products during which FDA review or approval of an ANDA or 505(b)(2) application is precluded. If the pioneer product is a New Chemical Entity, or NCE, the FDA is precluded for a period of five years from accepting for review an ANDA or 505(b)(2) application for the same chemical entity. Under NCE exclusivity, the FDA may accept an ANDA or 505(b)(2) application for review after four years, however, if that application contains a Paragraph IV certification challenging one of the pioneer's listed patents.

The Hatch Waxman Act also provides three years of exclusivity for applications containing the results of new clinical investigations (other than bioavailability studies) essential to the FDA's approval of new uses of approved products, such as new indications, dosage forms, strengths, or conditions of use. During this three-year exclusivity period, the FDA may review but not approve an ANDA or 505(b)(2) application for a product with the same conditions of use as supported by those new clinical investigations. This exclusivity will not necessarily prohibit the FDA from accepting or approving ANDAs or 505(b)(2) applications for other products containing the same active ingredient.

If an ANDA or 505(b)(2) application containing a Paragraph IV certification is accepted for filing by the FDA, the applicant must within 20 days provide notice to an NDA holder and patent owner that the application has been submitted and provide the factual and legal basis for the applicant's opinion that the patent is invalid or not infringed. An NDA holder or patent owner may then file suit against the ANDA or 505(b)(2) applicant for patent infringement. If a suit is filed within 45 days of receiving notice of the Paragraph IV certification, the FDA is precluded from approving the ANDA or 505(b)(2) application for a period of 30 months. The 30-month stay generally begins on the date of the receipt of notice by an NDA holder or patent owner. If the pioneer product has NCE exclusivity and the pioneer files suit against the ANDA or 505(b)(2) application during the fifth year of exclusivity, however, the 30-month stay will not be triggered until five years from the date of the reference drug's approval. The FDA may approve the proposed product before the expiration of the 30-month stay if a court finds the patent invalid or not infringed or if the court shortens the period because the parties have failed to cooperate in expediting the litigation.

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.

Good Manufacturing Practices

Drug 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 some states that require manufacturers and others to adopt new 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 NDA or other application, shut down manufacturing operations or withdraw approval of an NDA for that drug, or we may recall the drug from distribution. Noncompliance with cGMP or other requirements can result in issuance of warning letters, civil and criminal penalties, seizures and injunctive action.

Advertising and Promotion

The FDA closely regulates the labeling, marketing and promotion of drugs. 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 providers, 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 federal Anti-Kickback Statute prohibits persons and entities from, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for or recommending the purchase, lease or order of any item or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting some common activities from prosecution, the exemptions and safe harbors are drawn narrowly. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the statute has been violated.

The reach of the Anti-Kickback Statute was also broadened by the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the Affordable Care Act, which, among other things, amended the intent requirement of the federal Anti-Kickback Statute such 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. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. A claim includes "any request or demand" for money or property presented to the U.S. government. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been

prosecuted for causing false claims to be submitted because of the companies' marketing of products for unapproved, and thus non-reimbursable, uses. In addition, the federal Health Insurance Portability and Accountability Act of 1996, and its implementing regulations, or HIPAA, created federal criminal laws that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

Many states have similar fraud and abuse statutes or regulations, including, without limitation, laws analogous to the federal Anti-Kickback Statute and the federal False Claims Act, that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some of these state laws apply to a broader range of conduct and may not have the same exceptions as analogous federal laws. Accordingly, our business will be subject to these provisions as well in the states in which we do business.

The federal Physician Payments Sunshine Act, enacted as part of the Affordable Care Act requires applicable 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 track and annually report to the Centers for Medicare and Medicaid Service, or CMS, payments and other transfers of value provided to physicians and teaching hospitals and certain ownership and investment interests held by physicians or their immediate family members. If our operations are found to be in violation of any of such laws we may be subject to penalties, which could adversely affect our ability to operate our business and our financial results.

In addition, we may be subject to data privacy and data security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, imposes specified requirements relating to the privacy, security and transmission of certain individually identifiable health information. HIPAA applies to certain covered entity health care providers, health plans and health care clearinghouses as well as their business associates, which are entities that create, receive, maintain or transmit protected health information in connection with providing a service to or performing an activity for or on behalf of a covered entity. Violations of HIPAA may result in civil and/or criminal penalties and state attorneys' general have authority to file civil actions for damages or injunctions in federal courts to enforce HIPAA and seek attorney's fees and costs associated with pursuing federal civil actions. Even if we are not directly subject to HIPAA, we could be subject to criminal penalties if we knowingly obtain or disclose individually identifiable health information maintained by a HIPAA covered entity in a manner not authorized or permitted by HIPAA. In addition, state laws 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. 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, 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, any of which could adversely affect our ability to operate our business and our results of 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 EU Directive 95/46/EC 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 on any entity that manufactures or imports branded prescription drugs and biologic agents, apportioned among these entities according to their sales of branded prescription drugs under certain government healthcare programs, such as Medicare and Medicaid;
- increases in the statutory minimum rebates a manufacturer must pay as a condition to having covered drugs available for payment under the Medicaid Drug Rebate program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, and the addition of new government investigative powers and enhanced penalties for non-compliance;
- extension of a manufacturer’s Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- a new Medicare Part D coverage gap discount program, under which a participating manufacturer must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new eligibility categories for certain individuals with income at or below 133% of the federal poverty level;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, known as the 340B drug pricing program;
- the new requirements under the federal Open Payments program created as part of the Physician Payments Sunshine Act under Section 6002 of the Affordable Care Act and its implementing regulations, which requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program (with certain exceptions) to report annually to the 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. Applicable manufacturers and applicable group purchasing organizations must also report annually to the U.S.

Department of Health and Human Services ownership and investment interests held by physicians (as defined above) and their immediate family members. Covered manufacturers are required to submit data reports by the 90th day of each calendar year;

- 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 and amendments to continue. In January, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the Affordable Care Act. The Budget Resolution is not a law; however, it is widely viewed as the first step toward the passage of repeal legislation. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, on average, through 2025, which went into effect in April 2013. 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 bills 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. 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. For example, based on scientific advice from the European Medicines Agency, or the EMA, we believe our current clinical development plan is likely to be insufficient to receive regulatory approval in Europe. During the next year, we plan to work with the EMA to formulate a development plan that may be more acceptable, but may be unsuccessful in doing so or such plan may not be feasible. 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 7, 2017, we had 32 full-time employees and one part-time employee. Of the full-time employees, 19 were primarily engaged in research and development activities and ten 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.

Research and Development

We have dedicated a significant portion of our resources to our efforts to develop our product candidates, entinostat and SNDX-6352. We incurred research and development expenses of $31.7 million, $9.5 million and $10.2 million during the years ended December 31, 2016, 2015 and 2014, respectively. We anticipate that a significant portion of our operating expenses will continue to be related to research and development in 2017, as we continue to advance our product candidates through clinical development.

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 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, 2016, we reported a net loss of $44.5 million; and as of December 31, 2016, we had an accumulated deficit of $305.3 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 two product candidates, entinostat and SNDX-6352. 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 entinostat 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, entinostat or SNDX-6352 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 which 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 entinostat and SNDX-6352 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 entinostat and SNDX-6352. 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 entinostat 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 prevented from pursuing 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 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.

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 April 30, 2016 and determined that on March 30, 2007 and August 21, 2015 ownership changes had occurred. We may have experienced an ownership change subsequent to April 30, 2016; and 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.

Risks Related to Our Business and Industry

Entinostat and SNDX-6352 are currently our only product candidates. If we are unable to successfully complete clinical development of, obtain regulatory approval for and commercialize entinostat or SNDX-6352, our business prospects will be significantly harmed.

Entinostat and SNDX-6352 are currently our only product candidates. Our financial success will depend substantially on our ability to effectively and profitably commercialize entinostat and SNDX-6352. In order to commercialize entinostat and SNDX-6352, 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 entinostat and SNDX-6352 will depend on a number of factors, including the following:

- timely commencement and completion of the planned Phase 1b/2 clinical trial of entinostat in combination with avelumab and the Phase 1 clinical trial of SNDX-6352;
- completion of the planned Phase 1b/2 clinical trials of entinostat in combination with each of *Keytruda* and atezolizumab;
- timely patient enrollment and completion of the Phase 3 clinical trial in advanced HR+, HER2- breast cancer, which may be significantly slower than we currently anticipate and will depend substantially upon the satisfactory performance of the ECOG-ACRIN and the NCI and other third-party contractors for entinostat;
- whether we are required by the FDA or foreign regulatory authorities to conduct additional clinical trials;

- the prevalence and severity of adverse side effects;
- the ability to demonstrate safety and efficacy of entinostat and SNDX-6352 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 of entinostat and SNDX-6352, and to develop, validate and maintain a commercially viable manufacturing process that is compliant with cGMP;
- the availability of commercial supplies of therapeutics, including *Aromasin* and *Keytruda*, 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;
- 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 entinostat and SNDX-6352.

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 is clinically untested 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 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 immune checkpoint inhibitors and assess both the safety and efficacy of the combination of entinostat plus a checkpoint inhibitor. However, we have not yet demonstrated the safety or the benefit of this combination in humans and we may be unable to establish a clinically meaningful benefit for patient without added toxicity.

Although the NCI has entered into a 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 *Aromasin* in advanced HR+, HER2- breast cancer was reviewed and agreed upon by the FDA under an 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 a 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. Further, obtaining clinical trial data meeting the clinical endpoints 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 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.

If the Phase 3 clinical trial of entinostat in combination with Aromasin 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 *Aromasin* in advanced HR+, HER2- breast cancer patients. The trial will measure two primary endpoints of PFS, and overall survival. Based on information received from ECOG-ACRIN to date, PFS data is expected no sooner than the end of 2017 and overall survival data no sooner than the second half of 2019. If the Phase 3 clinical trial meets the PFS endpoint and the interim analysis of overall survival demonstrates a favorable trend, we expect to submit an NDA based on this data. However, if the trial does not meet the PFS endpoint, we will not be able to submit an NDA unless and until we receive data demonstrating that the primary endpoint for overall survival has been achieved. In addition, based on scientific advice from the European Medicines Agency, the current Phase 3 clinical trial is not likely to 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 *Aromasin*, we cannot be certain that we will not observe these toxicities or unexpected side effects 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 *Faslodex* 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 *Faslodex* and *Ibrance* 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 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 *Aromasin* 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 or not 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 does not successfully carry out its obligations and responsibilities or meet expected deadlines or if the quality or accuracy of the clinical data it obtains is compromised due to the failure to adhere to 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 you 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 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 *Aromasin* in advanced HR+, HER2- breast cancer commenced in the second quarter of 2014, and ECOG-ACRIN expects to have PFS data from this trial no sooner than the end of the second half of 2017. However, to date, ECOG-ACRIN's enrollment of patients in this trial has been slower than expected. We do not know whether this trial will need to be restructured, or will be completed on schedule or at all. Our product development costs will increase if we experience delays in clinical testing. 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 which may result in a delay or unsuccessful completion of clinical development of entinostat include, among other things:

- failure of ECOG-ACRIN to timely identify and enroll patients in the Phase 3 clinical trial;
- 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;
- unexpectedly high rate of patients withdrawing consent or being lost to follow-up;
- 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 side effects;
- failure to demonstrate the efficacy of entinostat in this clinical trial;
- inability to identify and maintain a sufficient number of clinical trial sites, many of which may already be engaged in other clinical trial programs, including some that may be for the same indication;
- withdrawal of clinical trial sites from our clinical trials as a result of changing standards of care or the ineligibility of a site to participate in our trials; 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.

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 with immuno-oncology agents;
- the size and nature of the patient population;
- 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 and Pfizer and any future collaborators to perform satisfactorily under our agreements.

Under the agreements with Merck, Genentech, Merck KGaA and Pfizer 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 and, 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 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 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. It is possible that any clinical trials conducted by KHK 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. For example, under the UCB license agreement, UCB is transferring to us certain data and materials, provide limited technical assistance and certain transitional services, and manufacture and supply us with a preliminary supply of SNDX-6352, which we expect will assist us with the development, manufacture and commercialization of SNDX-6352. If UCB fails to complete such technology transfer or to supply us with sufficient quantities of SNDX-6352, our efforts to develop and commercialization SNDX-6352 may be delayed or may fail. 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 is terminated, 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 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 a 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 entinostat and/or SNDX-6352 for a more limited patient population than we request, may grant approval contingent on the performance of costly post-marketing trials, may impose a 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 Aromasin, Keytruda, atezolizumab, avelumab 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 *Aromasin*, *Keytruda*, atezolizumab, avelumab 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 and the Phase 1b/2 clinical trials in NSCLC, melanoma, ovarian cancer and TNBC, and if entinostat receives regulatory approval, to commercialize entinostat for treatment of advanced HR+, HER2- breast cancer, NSCLC, melanoma, ovarian cancer or TNBC. A shortage of supply may also result in an increase, which could be significant, in our costs of procuring *Aromasin*.

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;
- the availability of coverage and adequate reimbursement and pricing by third parties and 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 entinostat and SNDX-6352. 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.

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 have received breakthrough therapy designation from the FDA for entinostat when used in combination with *Aromasin* based on the overall survival 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, if results from the Phase 3 clinical trial do not confirm the improvements in PFS or overall survival observed in our Phase 2b clinical trial, the FDA may rescind our breakthrough therapy designation.

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 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 its regulatory approval, limit the commercial scope of its 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

from the European Medicines Agency, 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, melanoma, ovarian cancer and TNBC patients includes chemotherapies and therapies targeting specific gene mutations. More recently, immune checkpoint inhibitors have been approved for NSCLC and melanoma and are under investigation for ovarian cancer and TNBC. There are currently no approved combination immuno-oncology therapies although numerous drugs are undergoing active clinical investigation. We believe that if entinostat in combination with either *Keytruda*, atezolizumab or avelumab were approved for the treatment of NSCLC, melanoma, TNBC or ovarian cancer, it would face competition from these standard-of-care approaches and other investigational drugs being tested in combination with any of these approaches.

If entinostat in combination with *Aromasin* 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*, *Afinitor*, and other therapies currently in Phase 3 clinical development such as abemaciclib, being developed by Eli Lilly and Company, and ribociclib and buparlisib, both of which are being developed by Novartis.

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 *Aromasin*, *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.

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 entinostat, 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 government healthcare programs, private health insurers, managed care plans and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, determine which medications they will cover and establish reimbursement levels. Government authorities and other 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 the CMS' decisions 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.

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 regulatory requirements, the FDA could take enforcement action that could jeopardize our ability to market the product candidate.

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. There have been judicial and Congressional challenges to certain aspects of the Affordable Care Act, and we expect there will be additional challenges and amendments in the future. In January, Congress voted to adopt a budget resolution for fiscal year 2017, or the Budget Resolution, that authorizes the implementation of legislation that would repeal portions of the Affordable Care Act. The Budget Resolution is not a law; however, it is widely viewed as the first step toward the passage of repeal legislation. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. We cannot predict how the Affordable Care Act, its possible repeal, or any legislation that may be proposed to replace the Affordable Care Act will impact our business.

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 has extended the 2% reduction to 2025. 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 bills 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.

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, imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- HIPAA imposes civil and criminal liability for, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense, knowingly and willfully making false statements relating to healthcare matters, or knowingly obtaining or disclosing individually identifiable health information maintained by a HIPAA-covered entity in a manner that is not authorized or permitted by HIPAA;
- 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 Open Payments program, created as part of the Physician Payments Sunshine Act under Section 6002 of the Affordable Care Act and its implementing regulations, 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 the U.S. Department of Health and Human Services 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 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, 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 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 expires in September 2017. We expect to seek extensions of patent terms where these are available in any countries where we are prosecuting patents. This includes in the United States 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. However, the applicable authorities, including the FDA in the United States, and any equivalent regulatory authorities in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case. Even if we submit an NDA before the expiration of U.S. Patent RE39,754 and are successful in obtaining an extension of the term of U.S. Patent RE39,754 based on FDA regulatory delays, such extension will only extend the term of RE39,754 for a few additional years (up to a maximum of five additional years for patent claims covering a new chemical entity).

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 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.

The portfolio 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.

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 $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. 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 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.

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 any 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.

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. 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 commence coverage of us, the trading price for our stock could be negatively impacted. In the event we obtain securities or industry analyst coverage, if any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our trials or operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

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

As of December 31, 2016, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially own approximately 74% of our outstanding voting stock. 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 will be able to 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 $1.0 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 intend to take advantage of some, but not all, of the reduced regulatory and reporting requirements that will be 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 will 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 incur increased costs as a result of operating as a public company, and our management will devote substantial time to new 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. Our management and other personnel needs to devote a substantial amount of time to these compliance initiatives. Moreover, we expect these rules and regulations to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. The increased costs will increase our net loss. For example, these rules and regulations have made it more difficult and more expensive for us to obtain director and officer liability insurance and we were required to incur substantial costs to maintain the sufficient coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

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:

- authorizing the issuance of "blank check" preferred stock, the terms of which we may establish and shares of which we may issue without stockholder approval;
- prohibiting cumulative voting in the election of directors, which would otherwise allow for less than a majority of stockholders to elect director candidates;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

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

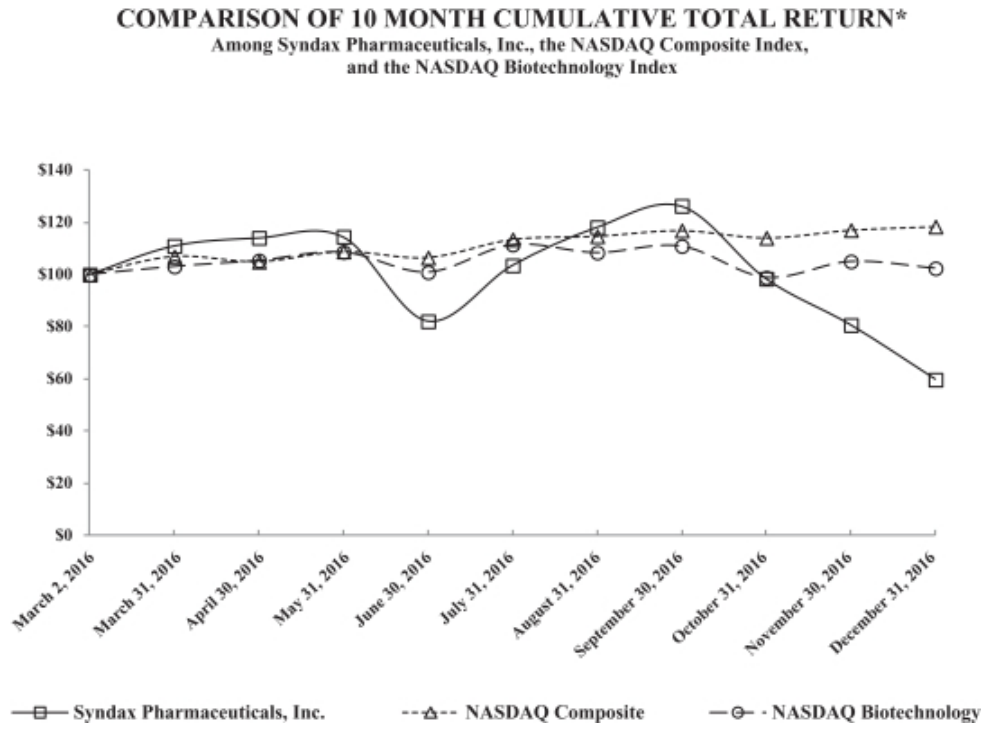
Our common stock began trading on the NASDAQ Global Select Market on March 2, 2016, under the symbol "SNDX." Prior to that time, there was no public market for our common stock. The following table sets forth the high and low closing sales prices per share of our common stock as reported on The NASDAQ Global Select Market for the periods indicated.

Year Ended December 31, 2016	High	Low
First Quarter (Beginning March 2, 2016)	$14.83	$11.00
Second Quarter	$16.60	$ 9.06
Third Quarter	$17.13	$ 9.80
Fourth Quarter	$16.07	$ 6.91

Comparative Stock Performance Graph

The following performance graph and related information shall not be deemed "soliciting material" or to be "filed" with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act or Exchange Act. The following graph shows a comparison from March 2, 2016 (the date our common stock commenced trading on the NASDAQ Global Select Market) through December 31, 2016, of the cumulative total return for our common stock, the NASDAQ Composite Index, and the NASDAQ Biotechnology

Index. The graph assumes an initial investment of $100 on March 2, 2016. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock.



* $100 invested on 3/2/16 in stock or 2/29/16 in index, including reinvestment of dividends.
Fiscalyear ending December 31.

	2-Mar-16	31-Mar-16	30-Apr-16	31-May-16	30-Jun-16	31-Jul-16	31-Aug-16	30-Sep-16	31-Oct-16	30-Nov-16	31-Dec-16
Syndax Pharmaceuticals, Inc.	$ 100.00	$ 111.00	$ 114.08	$ 114.50	$ 82.08	$ 103.50	$ 118.17	$ 126.33	$ 98.42	$ 80.67	$ 59.75
NASDAQ Composite	$ 100.00	$ 106.98	$ 104.96	$ 108.85	$ 106.51	$ 113.48	$ 114.72	$ 116.91	$ 114.08	$ 117.06	$ 118.41
NASDAQ Biotechnology	$ 100.00	$ 103.10	$ 105.39	$ 108.64	$ 100.90	$ 111.50	$ 108.44	$ 110.93	$ 98.87	$ 105.03	$ 102.40

Holders of Record

As of March 7, 2017, we had approximately 34 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. We invested the funds received in cash equivalents and other short-term investments in accordance with our investment policy. As of December 31, 2016, we have not used any of the proceeds from the IPO and as such, the entire amount of the net proceeds is included as cash, cash equivalents and short-term investments.

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, 2016, 2015, and 2014 and the consolidated balance sheet data as of December 31, 2016 and 2015, from our audited consolidated financial statements, included elsewhere in this Annual Report on Form 10-K. We have derived the consolidated balance sheet data as of December 31, 2014 from our audited financial statements not included in this report. 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:

(In thousands, except share and per share data)	Years Ended December 31, 2016	2015	2014
Revenue	$ 1,220	$ 627	$ —
Operating expenses:			
Research and development	31,665	9,549	10,175
General and administrative	13,321	11,591	11,157
Total operating expenses	44,986	21,140	21,332
Loss from operations	(43,766)	(20,513)	(21,332)
Interest income (expense)	956	(1,414)	(289)
Other (expense) income	(1,662)	(2,192)	1,793
Net loss	$ (44,472)	$ (24,119)	$(19,828)
Net loss attributable to common stockholders(1)	$ (47,070)	$ (103,845)	$(26,357)
Net loss per share attributable to common stockholders—basic and diluted(1)	$ (3.22)	$(1,519.27)	$(453.02)
Weighted-average common shares outstanding—basic and diluted(1)	14,619,716	68,352	58,181

Consolidated Balance Sheet Data:

(In thousands)	December 31, 2016	2015	2014
Cash, cash equivalents and short-term investments	$ 105,330	$ 86,489	$ 12,091
Working capital(2)	98,144	83,160	2,181
Total assets(2)	109,013	89,903	12,525
Convertible preferred stock	—	319,113	146,853
Accumulated deficit	(305,293)	(259,675)	(159,801)
Total stockholders' equity (deficit)	84,139	(252,415)	(152,569)

(1) See Note 4 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 Standards Update 2015-03, *Interest—Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs.* The impact of adoption was an increase of $83,000 in working capital and a decrease of $291,000 in total assets.

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 combination therapies in multiple cancer indications. Our lead product candidate, entinostat, is currently being evaluated in a Phase 3 clinical trial for HR+, HER2- breast cancer. Entinostat was granted Breakthrough Therapy designation by the FDA, following positive results from our Phase 2b clinical trial, ENCORE 301. We are developing entinostat, which has direct effects on both cancer cells and immune regulatory cells, and SNDX-6352, a monoclonal antibody that targets the colony stimulating factor-1 receptor, or CSF-1R, to enhance the body's immune response on tumors that have shown sensitivity to immunotherapy. We are evaluating entinostat as a combination therapeutic in Phase 1b/2 clinical trials with Merck for NSCLC and melanoma; with Genentech for TNBC; and with Merck KGaA and Pfizer for ovarian cancer. We acquired the exclusive rights to SNDX-6352 in July 2016 and are evaluating SNDX-6352 in a single ascending dose Phase 1 clinical trial. 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.

On February 24, 2016, we effected a 1-for-1.25 reverse stock split of our outstanding common stock and convertible preferred stock; on June 3, 2014, we effected a 1-for-12.3 reverse stock split of our outstanding common stock and convertible preferred stock; and on November 18, 2013, we effective a 1-for-10 reverse stock split of our outstanding common stock and convertible preferred stock. Stockholders entitled to fractional shares

as a result of the reverse stock splits received a cash payment in lieu of receiving fractional shares. All of our historical share and per share information shown in the accompanying financial statements and related notes have been retroactively adjusted to give effect to the reverse stock splits.

In March 2016, we completed our IPO, whereby we sold 4,809,475 shares of common stock at the initial public offering price of $12.00 per share, which included 409,475 shares issued pursuant to the underwriters' partial exercise of their over-allotment option to purchase additional shares of common stock. We received net proceeds of $50.5 million from the offering, after deducting underwriting discounts and commissions and other offering costs. Our shares trade on the Nasdaq Global Select Market under the symbol "SNDX."

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, 2016, 2015, and 2014, we reported a net loss of $44.5 million, $24.1 million and $19.8 million, respectively. As of December 31, 2016, we had an accumulated deficit of $305.3 million, which included non-cash charges for stock-based compensation, preferred stock accretion and extinguishment charges. As of December 31, 2016, we had cash, cash equivalents and short-term investments of $105.3 million.

Pipeline Updates

- E2112 is approximately 64% enrolled. Based upon current enrollment trends, ECOG-ACRIN anticipates enrollment could be completed and progression-free survival data available by the end of 2017.
- During the fourth quarter of 2016, we commenced the single ascending dose in the Phase 1 clinical trial of SNDX-6352 in healthy volunteers to determine the safety and pharmacokinetics of the anti-CSF-1R monoclonal antibody.
- We have completed enrollment of the three cohorts in the first stage of the Phase 2 component of ENCORE 601 in patients with melanoma and NSCLC. ENCORE 601 is an open-label, Phase 1b/2 clinical trial evaluating the combination of entinostat plus Merck's anti-PD-1 blocking therapy, *Keytruda*, in patients with melanoma and NSCLC to provide an initial efficacy signal across three defined patient populations. In February 2017, the melanoma cohort of the 601 trial met the pre-specified objective response threshold; and we progressed to the second stage of the trial. This cohort will now enroll an additional 21 patients. Data from Stage 1 of the other two cohorts is still maturing, and we expect to have a decision regarding a go/no go decision into Stage 2 for these cohorts in the first half of 2017.
- In June 2016, we initiated the Phase 1b portion of ENCORE 602 in patients with TNBC. This phase of the study completed enrollment during the fourth quarter of 2016, establishing the 5 mg weekly dose of entinostat safe to go forward in the recently initiated phase 2 portion of the trial.
- In collaboration with Merck KGaA and Pfizer, we initiated ENCORE 603 in January 2017 and expect safety data from the Phase 1b safety portion during the first half of 2017.

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, 2016 and 2015 have been solely derived from our license agreement with 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 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. The balance of the upfront payment of $7.7 million was allocated to KHK's purchase of shares of our Series B-1 convertible preferred stock. We did not have any revenue for the year ended December 31, 2014.

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 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, 2016, we have incurred $103.4 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 amounts borrowed under our term loan facility, capital leases and convertible notes.

Change in Fair Value of Common Stock Warrant Liability

The change in fair value of the common stock warrant liability was associated with a warrant to purchase common stock issued in connection with a license agreement and consisted of the calculated change in value based upon the fair value of the underlying security at the end of each reporting period as calculated using the Black-Scholes option pricing model. Gains and losses arising from changes in fair value were recognized in other income (expense) in the consolidated statement of operations. As of the closing of our IPO, the anti-dilution provision of the warrant expired; and the warrant liability was reclassified to additional paid-in capital.

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, liabilities and expenses and the disclosure of contingent assets and liabilities in our financial statements. On an ongoing basis, we evaluate our estimates and judgments, including those related to accrued research and development expenses and stock-based compensation. 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 Recognition

We have generated revenue through license fees for the development and commercialization our product candidate, entinostat. We make judgments that affect the periods over which we recognize revenue. We recognize revenue when (i) persuasive evidence of an arrangement exists; (ii) transfer of technology has been completed, services have been performed or products have been delivered; (iii) the fee is fixed and determinable; and (iv) collection is reasonably assured. For revenue agreements with multiple-elements, we identify the deliverables included within the agreement and evaluate which deliverables represent separate units of accounting based on the achievement of certain criteria including whether the deliverable has stand-alone value to the collaborator. Upfront payments received in connection with licenses of our technology rights are deferred if facts and circumstances dictate that the license does not have stand-alone value and are recognized as license revenue over the estimated period of performance that is generally consistent with the terms of the research and development obligations contained in the specific license agreement. We periodically review our estimated periods of performance based on the progress under each arrangement and account for the impact of any changes in estimated periods of performance on a prospective basis.

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 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.

Stock-Based Compensation

We issue stock-based awards to employees and non-employees, generally in the form of stock options. We account for our stock-based awards in accordance with FASB Accounting Standards Codification, or ASC, Topic 718, *Compensation—Stock Compensation*, or ASC 718. ASC 718 requires all stock-based payments to employees, including grants of employee stock options and modifications to existing stock options, to be recognized in the consolidated statement of operations based on their fair values on the date of grant. We account for stock-based awards to non-employees in accordance with FASB ASC Topic 505-50, *Equity-Based Payments to Non-Employees*, which requires the fair value of the award to be re-measured at fair value as the award vests. We recognize the compensation cost of service-based awards on a straight-line basis over the vesting period of the award for employees and non-employees, which is generally four years.

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 our IPO, the fair value of the common stock underlying the stock options had been determined by the board of directors 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. Following the completion of the IPO, stock option values are determined based on the market price of our common stock on the NASDAQ Global Select Market.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires the input of highly subjective assumptions, including the fair value of the underlying common stock, the expected volatility of the price of our common stock, the expected term of the option, and the risk-free interest rate. Prior to our IPO, we were a privately-held company and lacked company-specific historical and implied volatility information. Therefore, we estimated our expected volatility based on the historical volatility of our publicly traded peer companies. We expect to continue to do so until such time as we have adequate historical data regarding the volatility of our traded stock price following our IPO. We estimate the expected term of the options using the "simplified method," whereby the expected life equals the average of the vesting term and the original contractual term of the option. The risk-free interest rate is determined by reference to U.S. Treasury bond yields at or near the time of grant for time periods similar to the expected term of the award.

We are also required to estimate forfeitures at the time of grant and revise estimates in subsequent periods if actual forfeitures differ from estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from our estimates, the difference is recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the consolidated financial statements is based on awards that are ultimately expected to vest.

See Note 14 to our consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information on our stock-based compensation.

Derivative Instruments

We have recorded common stock warrants issued in connection with license agreements as derivative financial liabilities. These warrants were initially recorded at fair value with gains and losses arising from

changes in fair value recognized in the consolidated statement of operations at each period end while such instruments are outstanding. The liabilities were valued using a Black-Scholes option-pricing model. The significant assumptions used in estimating the fair value of our warrant liabilities include the exercise price, volatility of the stock underlying the warrant, risk-free interest rate, estimated fair value of the stock underlying the warrant, and the estimated life of the warrant.

In 2014, we recorded a derivative liability related to the 2014 term loans for the contingent success fee owed upon the occurrence of an IPO or other change of control events. The estimated fair value was determined using a PWERM approach. The fair value of the derivative was re-measured at each balance sheet date until the liability was settled and any changes in the fair value of the derivative liability were recorded in other income (expense) in the consolidated statement of operations. The term loans were paid in full in October 2015; however, the liability for the success fee survived the repayment of the term loans. Upon completion of the IPO, the success fee is no longer considered a derivative liability. The success fee of $0.2 million is payable by June 2018 and included in other long-term liabilities.

Results of Operations

Comparison of the years ended December 31, 2016 and 2015:

(in thousands)	Years Ended December 31, 2016	2015	Increase (Decrease) $	%
Revenues:				
License fees	$ 1,220	$ 627	$ 593	95%
Total revenues	1,220	627	593	95%
Operating expenses:				
Research and development	31,665	9,549	22,116	232%
General and administrative	13,321	11,591	1,730	15%
Total operating expenses	44,986	21,140	23,846	113%
Loss from operations	(43,766)	(20,513)	(23,253)	113%
Other (expense) income:				
Interest income (expense), net	956	(1,414)	2,370	(168)%
Change in fair value of common stock warrant liability	(1,703)	(2,155)	452	(21)%
Other income (expense), net	41	(37)	78	(211)%
Total other (expense) income	(706)	(3,606)	2,900	(80)%
Net loss	$ (44,472)	$ (24,119)	$ (20,353)	84%

License Fees

For the year ended December 31, 2016, license fees increased $0.6 million, or 95%, to $1.2 million compared to $0.6 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.

Research and Development

For the year ended December 31, 2016, our total research and development expenses increased $22.1 million, or 232%, to $31.7 million from $9.5 million for the prior year. These increases were primarily due

to increased patient accrual costs in E2112, higher expenses associated with the Phase 2 expansion of ENCORE 601, and the commencement of ENCORE 602 as well which represented an overall all increase in clinical and research activities of $13.5 million as well as the $5 million upfront payment related to expanding the pipeline with SNDX-6352. In addition, there were also increases in employee compensation costs of $2.4 million, legal and consulting activities of $0.6 million, facilities costs of $0.4 million and travel costs of 0.1 million. The increase in employee compensation costs was primarily due to on-boarding expenses of $2.2 million related to 14 additional employees, restructuring costs of $0.1 million, and non-cash stock-based compensation expense of $0.1 million.

Research and development expenses consisted of the following:

	Years Ended December 31,		Increase (Decrease)	
(in thousands)	2016	2015	$	%
External research and development expenses	$25,236	$5,957	$19,279	324%
Internal research and development expenses	6,429	3,592	2,837	79%
Total research and development expenses	$31,665	$9,549	$22,116	232%

General and Administrative

For the year ended December 31, 2016, our total general and administrative expenses increased $1.7 million, or 15%, to $13.3 million, from $11.6 million for the prior year. The increase in general and administrative expenses was primarily due to increases in employee compensation of $1.3 million, directors and officers insurance and other costs related to being a public company of $1.0 million, and facilities costs of $0.2 million. These increases were partially offset by decreases in legal and consulting expenses of $0.8 million primarily due to lower patent legal costs and lower spending related to market research during 2016 compared to 2015. 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 $0.8 million. These increases were partially offset by a decrease in restructuring costs of $0.6 million.

Interest Income (Expense), Net

For the year ended December 31, 2016, interest income (expense), net, increased $2.4 million from the prior year. The increase was primarily due to interest earned on our cash, cash equivalents and short-term investments of $0.9 million in 2016 compared to $0.5 million in 2015, which increased as a result of the $50.5 million of net proceeds from our IPO in March 2016 and $79.6 million of net proceeds from our Series C-1 preferred stock financing during the second and third quarters of 2015. In addition, for 2015, interest income (expense), net, included interest expense on the $9.0 million of term loans that were funded in December 2014. The term loans were paid in full in October 2015, and there was no interest-bearing debt outstanding as of December 31, 2016 and December 31, 2015.

Change in Fair Value of Common Stock Warrant Liability

The decrease in expense of $0.5 million in the change in fair value of common stock warrant liability for the year ended December 31, 2016, compared to the prior year was due to the expiration of the anti-dilution provision contained in the Bayer warrant as a result of the closing of our IPO during the first quarter of 2016, upon which the warrant liability was reclassified to additional paid-in capital.

Comparison of the years ended December 31, 2015 and 2014:

(in thousands)	Years Ended December 31, 2015	2014	Increase (Decrease) $	%
Revenues:				
License fees	$ 627	$ —	$ 627	100%
Total revenues	627	—	627	100%
Operating expenses:				
Research and development	9,549	10,175	(626)	(6)%
General and administrative	11,591	11,157	434	4%
Total operating expenses	21,140	21,332	(192)	(1)%
Loss from operations	(20,513)	(21,332)	(819)	(4)%
Other (expense) income:				
Interest (expense) income, net	(1,414)	(289)	1,125	NM
Change in fair value of common stock warrant liability	(2,155)	1,789	3,944	NM
Other (expense) income, net	(37)	4	41	NM
Total other (expense) income	(3,606)	1,504	5,110	NM
Net loss	$(24,119)	$(19,828)	$4,291	22%

License Fees

For the year ended December 31, 2015, we recognized license fees of $0.6 million derived from the KHK license agreement. The arrangement consideration of $17.3 million was allocated to the license unit of accounting and will be 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. In June 2015, we began delivering clinical supplies to KHK and commenced recognizing revenue.

Research and Development

For the year ended December 31, 2015, our total research and development expenses decreased $0.6 million, or 6%, to $9.5 million from $10.2 million for the prior year. Research and development for the year ended December 31, 2014, included the achievement of a $2.0 million development milestone under the license agreement with Bayer Pharma AG (formerly known as Bayer Schering Pharma AG), or Bayer, and the expenses related to the suspension of the planned 305 clinical trial in the third quarter of 2014. In addition, for the year ended December 31, 2015, spending related to the Phase 3 clinical trial of entinostat increased $0.8 million, expenses related to producing entinostat and placebo for clinical trials increased by $0.5 million, spending related to the ENCORE 601 trial increased $0.8 million and employee compensation costs increased $0.5 million. The increase in employee compensation costs was primarily due to non-cash charges related to stock-based compensation.

Research and development expenses consisted of the following:

(in thousands)	Years Ended December 31, 2015	2014	Increase (Decrease) $	%
External research and development expenses	$5,957	$ 7,241	$(1,284)	(18)%
Internal research and development expenses	3,592	2,934	658	22%
Total research and development expenses	$9,549	$10,175	$ (626)	(6)%

General and Administrative

For the year ended December 31, 2015, our total general and administrative expenses increased $0.4 million, or 4%, to $11.6 million, from $11.2 million for the prior year. The increase in general and administrative expenses was primarily due to the increases in compensation costs of $3.0 million and legal and consulting costs of $1.5 million for the year ended December 31, 2015, which was partially offset by the write-off of previously capitalized costs of $4.3 million incurred in connection with preparing for an IPO in September 2014. The increase in compensation costs was due to costs related to an increase in headcount as well as employee termination costs of $1.3 million, including $0.7 million of non-cash charges related to stock-based compensation. The increase in legal and consulting costs was primarily related to business development activities and intellectual property and trademark filings.

Interest (Expense) Income, Net

For the year ended December 31, 2015, interest expense, net, increased $1.1 million from the prior year. The increase was primarily due to interest expense on the $9.0 million of term loans that were funded in September and December 2014.

Change in Fair Value of Common Stock Warrant Liability

The increase in expense of $3.9 million in the change in fair value of common stock warrant liability for the year ended December 31, 2015 compared to the prior year was due to an increase in the fair value of the Bayer common stock warrant liability. At each period end, the fair value of the outstanding common stock warrant liability is re-measured, and the change in the fair value is recorded in other income (expense) in the consolidated statement of operations. Upon the completion of our IPO, the warrant was reclassified to additional paid-in capital.

Liquidity and Capital Resources

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. Since our inception and through December 31, 2016, our operations have been financed primarily by net proceeds from the sale of convertible preferred stock and convertible debt securities and proceeds from our license agreements. As of December 31, 2016, our cash, cash equivalents and short-term investments were $105.3 million. We believe that our existing cash, cash equivalents and short-term investments will be sufficient to fund our projected operating expenses and capital expenditure requirements for at least the next 12 months.

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, 2016, we had an accumulated deficit of $305.3 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, 2016	2015	2014
Net cash used in operating activities	$(35,157)	$ (2,428)	$(14,393)
Net cash (used in) provided by investing activities	(18,380)	(61,669)	1,888
Net cash provided by financing activities	54,202	77,267	12,410
Net increase (decrease) in cash and cash equivalents	$ 665	$ 13,170	$ (95)

Net Cash Used in Operating Activities

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 used in operating activities for the year ended December 31, 2015 was $2.4 million and primarily consisted of our net loss of $17.0 million adjusted for non-cash items including stock-based compensation of $3.9 million, the change in fair value of warrants of $2.1 million, amortization of debt discount and debt issuance costs of $0.8 million, and amortization and accretion of investments of $0.3 million and a net increase in operating assets and liabilities of $14.6 million. The significant items in the increase in operating assets and liabilities include increases in deferred revenue of $16.7 million and accounts payable of $1.0 million partially offset by an increase in prepaid expenses and other assets of $1.2 million and a decrease in accrued expenses and other liabilities of $1.9 million. The increase in deferred revenue of $16.7 million was due to the proceeds we received during the first quarter of 2015 from the KHK license agreement related to the upfront license fee of $17.3 million, net of license fee revenue recognized during the year ended December 31, 2015.

Net cash used in operating activities for the year ended December 31, 2014 was $14.4 million and primarily consisted of our net loss for the year ended December 31, 2014 of $14.9 million adjusted for non-cash items including stock-based compensation of $2.3 million, and the write-off of deferred costs associated with our postponed IPO, partially offset by the change in fair of warrants of $1.8 million and a net increase in operating assets and liabilities of $0.6 million. The significant items in the increase in operating assets and liabilities include an increase an increase in accrued expenses and other liabilities of $1.2 million, partially offset by a decrease in accounts payable of $0.7 million.

Net Cash (Used in) Provided by Investing Activities

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 used in investing activities for the year ended December 31, 2015 was $61.7 million and was primarily due to the purchase of $102.0 million of available-for-sale marketable securities partially offset by $40.5 million in proceeds from the maturities of available-for-sale marketable securities and an increase in restricted cash of $0.1 million.

Net cash provided by investing activities for the year ended December 31, 2014 was $1.9 million and was primarily due to the $5.3 million in proceeds from the maturities of available-for-sale marketable securities partially offset by the purchase of $3.4 million of available-for-sale marketable securities.

Net Cash Provided by Financing Activities

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.

Net cash provided by financing activities for the year ended December 31, 2015 was $77.3 million and was primarily due to the proceeds from the KHK license agreement and stock purchase agreement with KHK, of which $7.7 million related to the issuance of Series B-1 convertible preferred stock, and proceeds from the Series C-1 financings of $79.6 million, net of $0.4 million of issuance costs, partially offset by the $9.0 million early repayment of the term loans during the fourth quarter of 2015.

Net cash provided by financing activities for the year ended December 31, 2014 was $12.4 million and was primarily due to the $9.0 million proceeds from the term loans and $5.0 million from the issuance of convertible debt in the form of convertible notes, partially offset by $1.6 million of deferred issuance costs related to preparing for an IPO in 2014 and debt issuances.

Contractual Obligations and Commitments

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

(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)	$2,518	$ 393	$1,087	$979	$ 59
Operating lease for office equipment(2)	13	3	6	4	—
Capital lease for office equipment(3)	7	4	3	—	—
	$2,538	$ 400	$1,096	$983	$ 59

(1) In December 2013, we entered into a 40-month non-cancelable operating lease for office space in Waltham, Massachusetts, that expires on April 10, 2017. 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 new 62-month building lease for office space in New York, New York, which commenced on January 1, 2016. We have the right to terminate the New York lease after 38 months as long as proper notice is given and a termination fee equal to three months' rent is paid on the lease termination date. 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 December 2013, we entered into a five-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, 2016, we had federal and state tax net operating loss carryforwards of $36.0 million and $27.5 million, respectively. The federal and state net operating loss carryforwards expire at various dates through 2036. At December 31, 2016, we had available income tax credits of $2.0 million, 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 $1.0 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, 2016, we had cash equivalents of $23.8 million, consisting of overnight investments, interest-bearing money market funds and highly rated corporate bonds, and short-term investments of $81.5 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, 2016, 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

This Annual Report on Form 10-K does not include a report of management's assessment regarding our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) or an attestation report of our independent registered accounting firm due to a transition period established by rules of the Securities and Exchange Commission for newly public companies. Additionally, our auditors will not be required to formally opine on the effectiveness of our internal control over financial reporting pursuant to Section 404 until we are no longer an "emerging growth company" as defined in the JOBS Act as we have taken advantage of the exemptions available to us through the JOBS Act.

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 “Executive Officers” and “The Board of Directors and Its Committees” in our 2017 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 2017 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 2017 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 “Certain Relationships and Related Party Transactions” in our 2017 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” in our 2017 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.

The exhibits required to be filed as part of this Annual Report on Form 10-K are listed in the Exhibit Index attached hereto and are filed or incorporated herein by reference.

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 14, 2017

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. Briggs W. Morrison, M.D.	Chief Executive Officer and Director (Principal Executive Officer)	March 14, 2017
/s/ Richard P. Shea Richard P. Shea	Chief Financial Officer and Treasurer (Principal Financial Officer and Principal Accounting Officer)	March 14, 2017
/s/ Dennis G. Podlesak Dennis G. Podlesak	Chairman of the Board of Directors	March 14, 2017
/s/ Kim Kamdar, Ph.D. Kim Kamdar, Ph.D.	Director	March 14, 2017
/s/ Ivor Royston, M.D. Ivor Royston, M.D.	Director	March 14, 2017
/s/ Pierre Legault Pierre Legault	Director	March 14, 2017
/s/ Henry Chen Henry Chen	Director	March 14, 2017

Signature	Title	Date
/s/ Luke Evnin, Ph.D. Luke Evnin, Ph.D.	Director	March 14, 2017
/s/ Fabrice Egros, PharmD, Ph.D. Fabrice Egros, PharmD, Ph.D.	Director	March 14, 2017
/s/ George W. Sledge, Jr., M.D. George W. Sledge, Jr., M.D.	Director	March 14, 2017

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.
Waltham, Massachusetts

We have audited the accompanying consolidated balance sheets of Syndax Pharmaceuticals, Inc. and subsidiaries (the "Company") as of December 31, 2016 and 2015, 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, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, 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. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Syndax Pharmaceuticals, Inc. and subsidiaries as of December 31, 2016 and 2015, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2016, in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 14, 2017

SYNDAX PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2016	December 31, 2015
ASSETS		
Current assets:		
Cash and cash equivalents	$ 23,844	$ 23,179
Restricted cash	151	54
Short-term investments	81,486	63,310
Prepaid expenses and other current assets	3,029	1,464
Total current assets	108,510	88,007
Property and equipment, net	260	88
Other assets	243	1,808
Total assets	$ 109,013	$ 89,903
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 2,375	$ 1,452
Accrued expenses and other current liabilities	6,771	2,175
Current portion of deferred revenue	1,220	1,220
Total current liabilities	10,366	4,847
Long-term liabilities:		
Common stock warrant liability	—	2,848
Deferred revenue, less current portion	14,220	15,440
Other long-term liabilities	288	70
Total long-term liabilities	14,508	18,358
Total liabilities	24,874	23,205
Commitments (Note 16)		
Convertible preferred stock (Note 12)	—	319,113
Stockholders' equity (deficit):		
Series A convertible preferred stock, $0.001 par value, 0 and 3,512,194 shares authorized; 0 and 700,435 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively	—	7,231
Preferred stock, $0.001 par value, 10,000,000 and 0 shares authorized; 0 shares outstanding at December 31, 2016 and December 31, 2015, respectively	—	—
Common stock, $0.0001 par value, 100,000,000 and 20,800,000 shares authorized; 18,215,181 and 85,440 shares outstanding at December 31, 2016 and December 31, 2015, respectively	2	1
Additional paid-in capital	389,374	—
Accumulated other comprehensive income	56	28
Accumulated deficit	(305,293)	(259,675)
Total stockholders' equity (deficit)	84,139	(252,415)
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 109,013	$ 89,903

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,		
	2016	2015	2014
Revenues:			
License fees	$ 1,220	$ 627	$ —
Total revenues	1,220	627	—
Operating expenses:			
Research and development	31,665	9,549	10,175
General and administrative	13,321	11,591	11,157
Total operating expenses	44,986	21,140	21,332
Loss from operations	(43,766)	(20,513)	(21,332)
Other (expense) income:			
Interest income (expense), net	956	(1,414)	(289)
Change in fair value of common stock warrant liability	(1,703)	(2,155)	1,789
Other income (expense), net	41	(37)	4
Total other (expense) income	(706)	(3,606)	1,504
Net loss	$ (44,472)	$ (24,119)	$(19,828)
Net loss attributable to common stockholders	$ (47,070)	$ (103,845)	$(26,357)
Net loss per share attributable to common stockholders—basic and diluted	$ (3.22)	$(1,519.27)	$(453.02)
Weighted-average common shares outstanding—basic and diluted	14,619,716	68,352	58,181

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,		
	2016	2015	2014
Net loss	$(44,472)	$(24,119)	$(19,828)
Other comprehensive loss:			
Unrealized gains on marketable securities, net of tax	28	28	—
Comprehensive loss	$(44,444)	$(24,091)	$(19,828)

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

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 Capital	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount				
BALANCE—January 1, 2014	6,105,956	$ 140,324	700,435	$ 7,231	56,573	$ 1	$ —	$ —	$ (135,707)	$ (128,475)
Exercise of stock options	—	—	—	—	1,944	—	6	—	—	6
Accretion for convertible preferred stock dividends	—	6,529	—	—	—	—	(2,263)	—	(4,266)	(6,529)
Stock-based compensation expense	—	—	—	—	—	—	2,257	—	—	2,257
Net loss and comprehensive loss	—	—	—	—	—	—	—	—	(19,828)	(19,828)
BALANCE—December 31, 2014	6,105,956	146,853	700,435	7,231	58,517	1	—	—	(159,801)	(152,569)
Issuance of Series B-1 convertible preferred stock in January 2015 in conjunction with KHK Agreement	536,049	7,713	—	—	—	—	—	—	—	—
Issuance of Series C-1 convertible preferred stock in June 2015, net of issuance costs of $0.2 million	1,340,113	18,526	—	—	—	—	—	—	—	—
Conversion of 2014 Notes into Series C-1	372,446	5,211	—	—	—	—	—	—	—	—
Issuance of Series C-1 convertible preferred stock in August 2015, net of issuance costs of $0.2 million	4,377,902	61,084	—	—	—	—	—	—	—	—
Accretion of convertible preferred stock to redemption value	—	69,715	—	—	—	—	(123)	—	(69,592)	(69,715)
Accretion for convertible preferred stock dividends	—	10,011	—	—	—	—	(3,848)	—	(6,163)	(10,011)
Exercise of stock options	—	—	—	—	24,876	—	75	—	—	75
Vesting of restricted stock	—	—	—	—	2,047	—	14	—	—	14
Stock-based compensation expense	—	—	—	—	—	—	3,882	—	—	3,882
Unrealized gain on short-term investments	—	—	—	—	—	—	—	28	—	28
Net loss	—	—	—	—	—	—	—	—	(24,119)	(24,119)
BALANCE—December 31, 2015	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
Coversion 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

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,		
	2016	2015	2014
CASH FLOWS FROM OPERATING ACTIVITIES:			
Net loss	$ (44,472)	$ (24,119)	$(19,828)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	89	21	15
Amortization of debt discount and debt issuance costs	—	762	40
Amortization and accretion of investments	(126)	303	46
Stock-based compensation	4,708	3,882	2,257
Change in fair value of warrants	1,703	2,155	(1,789)
Write-off of deferred costs associated with postponed initial public offering	—	—	4,319
Other	25	8	(4)
Changes in operating assets and liabilities:			
Prepaid expenses and other assets	(1,629)	(1,205)	64
Accounts payable	923	1,045	(726)
Deferred revenue	(1,220)	16,660	—
Accrued expenses and other liabilities	4,842	(1,940)	1,213
Net cash used in operating activities	(35,157)	(2,428)	(14,393)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchases of property and equipment	(261)	(49)	(4)
Change in restricted cash	(97)	(118)	(1)
Purchases of short-term investments	(158,319)	(102,008)	(3,393)
Proceeds from sales and maturities of short-term investments	140,297	40,506	5,286
Net cash (used in) provided by investing activities	(18,380)	(61,669)	1,888
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issuance of common stock in initial public stock offering, net	52,148	—	—
Proceeds from issuance of convertible preferred stock, net	—	87,323	—
Proceeds from issuance of debt	—	—	14,000
Proceeds from exercise of stock options	2,058	191	6
Deferred issuance costs	—	(1,245)	(1,594)
Payments on term loans	—	(9,000)	—
Other	(4)	(2)	(2)
Net cash provided by financing activities	54,202	77,267	12,410
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	665	13,170	(95)
CASH AND CASH EQUIVALENTS—beginning of year	23,179	10,009	10,104
CASH AND CASH EQUIVALENTS—end of year	$ 23,844	$ 23,179	$ 10,009

Supplemental disclosures of cash flow information (Note 17).

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business

Syndax Pharmaceuticals, Inc. (the Company) is a clinical stage biopharmaceutical company developing an innovative pipeline of combination therapies in multiple cancer indications. The Company's lead product candidate, entinostat, is currently being evaluated in a Phase 3 clinical trial for advanced hormone receptor positive, human epidermal growth factor receptor 2 negative breast cancer. Entinostat was granted Breakthrough Therapy designation by the U.S. Food and Drug Administration following positive results from the Company's Phase 2b clinical trial, ENCORE 301. The Company is developing entinostat, which has direct effects on both cancer cells and immune regulatory cells, and SNDX-6352, a monoclonal antibody that targets the colony stimulating factor-1 receptor to enhance the body's immune response on tumors that have shown sensitivity to immunotherapy. The Company is evaluating entinostat as a combination therapeutic in Phase 1b/2 clinical trials with Merck & Co., Inc. for non-small cell lung cancer and melanoma; with Genentech, Inc. for triple negative breast cancer; and with Merck KGaA, Darmstadt, Germany, and Pfizer Inc. for ovarian cancer. We acquired the exclusive rights to SNDX-6352 in July 2016 and are evaluating SNDX-6352 in a single ascending dose Phase 1 clinical trial. 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, which included 409,475 shares issued pursuant to the underwriters' partial exercise of their over-allotment option to purchase additional shares of common stock. The aggregate net proceeds received by the Company from the offering were $50.5 million, net of underwriting discounts and commissions of $4.0 million and offering expenses of $3.1 million. Upon the closing of the IPO, all outstanding shares of the Company's outstanding convertible preferred stock converted into 12,872,551 shares of common stock; and the Company's outstanding warrant liability to purchase 357,840 shares of the Company's common stock valued at $4.6 million was reclassified to additional paid-in capital. The shares trade on the Nasdaq Global Select Market under the symbol "SNDX." 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, both of which were approved by the Company's board of directors and stockholders on September 28, 2015 and February 24, 2016, respectively. Pursuant to the amended and restated certificate of incorporation, the Company is now authorized to issue 100,000,000 shares of common stock and 10,000,000 shares of preferred stock.

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 either entinostat or SNDX-6352 is approved, if ever, and the Company begins to generate revenue from sales of entinostat and SNDX-6352. Accordingly, management expects to incur substantial losses on the ongoing development of entinostat and SNDX-6352 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, 2016 should enable the Company to maintain its planned operations for at least the next 12 months. 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").

On February 24, 2016, the Company effected a 1-for-1.25 reverse stock split of the Company's outstanding common stock and convertible preferred stock; and on June 3, 2014, the Company effected a 1-for-12.3 reverse stock split of the Company's outstanding common stock and convertible preferred stock. Stockholders entitled to fractional shares as a result of the reverse stock splits received a cash payment in lieu of receiving fractional shares. All of the Company's historical share and per share information shown in the accompanying financial statements and related notes have been retroactively adjusted to give effect to these reverse stock splits.

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 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. 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. Investments with remaining maturities or that are due within one year from the balance sheet date are classified as current.

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.

Other Assets

Other assets consist of deferred issuance costs, long-term security deposits, and noncurrent restricted cash. Deferred issuance costs consist primarily of direct incremental legal and accounting fees relating to the Company's IPO. As of December 31, 2016 and 2015, the Company had capitalized deferred IPO issuance costs of $0 and $1.6 million, respectively. Upon the closing of the IPO, these costs were reclassified to additional paid-in capital as a reduction of the IPO proceeds.

In September 2014, the Company determined that it was likely its IPO would be postponed for a period in excess of 90 days. As a result, in accordance with the Securities and Exchange Commission guidance in Staff Accounting Bulletin Topic 5-A, *Expenses of Offering*, the Company expensed as general and administrative expenses previously deferred IPO costs of $4.3 million.

Concentrations of Credit Risk

Cash and cash equivalents, restricted cash, and short-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 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 crdit 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 enters into license agreements for the development and commercialization of its product candidates, entinostat and SNDX-6352. 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 with the collaboration partners.

Revenue is recognized when (i) persuasive evidence of an arrangement exists, (ii) transfer of technology has been completed, services have been performed or products have been delivered, (iii) the fee is fixed and determinable, and (iv) collection is reasonably assured. For revenue agreements with multiple-elements, the Company identifies the deliverables included within the agreement and evaluates which deliverables represent separate units of accounting based on the achievement of certain criteria including whether the deliverable has stand-alone value. Upfront payments received in connection with licenses of the Company's technology rights are deferred if facts and circumstances dictate that the license does not have stand-alone value and are recognized as license revenue over the estimated period of performance that is generally consistent with the terms of the research and development obligations contained in the specific license agreement.

The Company periodically reviews its estimated periods of performance based on the progress under each arrangement and accounts for the impact of any changes in estimated periods of performance on a prospective basis. At the inception of each agreement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. The Company evaluates factors such as the scientific, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required to achieve the respective milestone and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. Non-refundable payments that are contingent upon achievement of a substantive milestone are recognized in their entirety in the period in which the milestone is achieved, assuming all other revenue recognition criteria are met. Other contingent payments in which a portion of the milestone consideration is refundable or adjusts based on future performance or non-performance (e.g., through a penalty or claw-back provision) are not considered to relate solely to past performance, and therefore, not considered substantive. Amounts that are not recognized as revenue due to the uncertainty as to whether they will be retained or because they are expected to be refunded are recorded as a liability. The Company recognizes non-substantive milestone payments over the remaining estimated period of performance once the milestone is achieved. Contingent payments associated with the achievement of specific objectives in certain contracts that are not considered substantive because the Company does not contribute effort to the achievement of such milestones are recognized as revenue upon achievement of the objective, as long as there are no undelivered elements remaining and no continuing performance obligations by the Company, assuming all other revenue recognition criteria are met.

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 expense 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, 2016, the Company incurred $0.5 million in external costs related to cost-sharing collaborations, of which $0.3 million has been recorded as a reduction to research and development expense. There were no cost-sharing arrangements in 2015 or 2014.

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 16) 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, 2016, 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, net of estimated forfeitures. Stock option awards to non-employees are subject to periodic revaluation over their vesting terms.

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.

Debt Discount

The Company has recorded the fair value of the derivative liability related to its term loans as debt discount, which is presented in the consolidated balance sheets as an offset to the carrying value amount of the debt. Debt discount is amortized to interest expense using the effective interest rate method or a method that approximates the effective interest rate method over the expected period that the debt is expected to be outstanding. In October 2015, the Company prepaid the outstanding balance on the term loans and wrote off the unamortized debt discount related to the term loans.

Derivative Liabilities

The Company records potential payments that would be made to lenders upon certain triggering events as derivative financial liabilities. The derivative liability is initially valued at fair value using a probability-weighted expected return model. Gains and losses arising from changes in fair value are recognized in other income (expense) in the consolidated statement of operations at each period end while such liabilities are outstanding.

Common Stock Warrants

The Company has recorded common stock warrants issued with license agreements as derivative financial liabilities, as the terms of the warrants are not fixed due to potential adjustments in the exercise price and/or the number of shares issuable under the warrants. The common stock warrants are initially recorded at fair value, with gains and losses arising from changes in fair value recognized in other income (expense) in the consolidated statement of operations at each period end while such instruments are outstanding. The warrant liabilities were valued using a Black-Scholes option-pricing model. Upon the closing of the IPO, the Company's outstanding warrant liability was reclassified to additional paid-in capital.

Recently Issued and Adopted Accounting Pronouncements

In November 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") 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. For public business entities, this ASU is effective for fiscal years beginning after December 15, 2017. The Company does not expect the adoption of this standard to have a material impact on its consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09, *Compensation—Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09"). ASU 2016-09 simplifies several aspects related to the accounting for share-based payment transactions, including the accounting for income taxes, forfeitures, statutory tax withholding requirements and classification on the statement of cash flows. ASU 2016-09 will be effective for the Company on January 1, 2017. The Company does not expect the adoption of this standard to have a material impact on its consolidated financial statements.

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. This ASU is effective for public reporting companies for interim and annual periods beginning after December 15, 2018, with early adoption permitted, and must be adopted using a modified retrospective approach. The standard will be effective for the Company on January 1, 2019. The Company is in the process of evaluating the effect of the new guidance on the Company's consolidated financial statements and related disclosures.

In August 2014, FASB issued ASU 2014-15, *Presentation of Financial Statements-Going Concern* ("ASU 2014-15"). ASU 2014-15 provides guidance on management's responsibility in evaluating whether there are conditions or events that raise substantial doubt about a company's ability to continue as a going concern within one year from the date the financial statements are issued, and about related footnote disclosures. ASU 2014-15 is effective for the annual period ending after December 15, 2016, and for annual periods and interim periods thereafter. The Company adopted ASU 2014-15 for the year ended December 31, 2016, and the adoption of this standard did not impact the Company's consolidated financial statements and related disclosures.

In May 2014, the FASB issued ASU 2014-09, *Revenue from Contracts with Customers* ("ASU 2014-09"). ASU 2014-09 supersedes the revenue recognition requirements of FASB Accounting Standards Codification ("ASC") Topic 605, *Revenue Recognition* and most industry-specific guidance throughout the Accounting Standards Codification, resulting in the creation of FASB ASC Topic 606, *Revenue from Contracts with Customers*. ASU 2014-09 requires entities to recognize revenue in a way that depicts the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled to in exchange for those goods or services. Adoption will be permitted using either a retrospective or modified retrospective approach. In July 2015, FASB voted to delay the effective date of the standard by one year to the first quarter of 2018 to provide companies sufficient time to implement the standard. Early adoption will be permitted, but not before the first quarter of 2017. The Company is currently evaluating the method by which it will implement this standard and the impact of the adoption of this standard on the Company's consolidated financial statements.

4. 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, 2016, 2015, and 2014, 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,		
	2016	2015	2014
Numerator—basic and diluted:			
Net loss	$ (44,472)	$ (24,119)	$(19,828)
Accretion of convertible preferred stock dividends	(2,598)	(10,011)	(6,529)
Accretion of convertible preferred stock to redemption value	—	(69,715)	—
Net loss attributable to common stockholders—basic and diluted	$ (47,070)	$ (103,845)	$(26,357)
Net loss per share—basic and diluted	$ (3.22)	$(1,519.27)	$(453.02)
Denominator—basic and diluted:			
Weighted-average common shares used to compute net loss per share—basic and diluted	14,619,716	68,352	58,181

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,		
	2016	2015	2014
Convertible preferred stock	—	12,872,551	6,246,041
Options to purchase common stock	2,560,737	2,606,195	831,148
Common stock warrant	357,840	277,486	127,099
Convertible notes and related accrued interest	—	—	363,294
Restricted stock subject to future vesting	8,542	14,684	—

5. Significant Agreements

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 of these findings, the upfront payment of $5.0 million has been 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 a license agreement (the "KHK 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. 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 of 536,049 shares of Series B-1 convertible preferred stock 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 purchase of the Series B-1 and the up-front payment of the license fee were accounted for separately. The Company allocated the amount of consideration related to Series B-1 equal to the fair value of the Series B-1 shares on the Effective Date based on a share price of $14.39 per share, which resulted in $7.7 million of proceeds allocated to the Series B-1 and the remaining consideration of $17.3 million allocated to the up-front license fee. The fair value of the Series B-1 of $14.39 per share was based on a contemporaneous valuation. The Company received $7.5 million and issued the Series B-1 in January 2015 and received the remaining $17.5 million in February 2015. On the date of issuance, the Company recorded accretion of $5.4 million to record the Series B-1 at its redemption value.

The Company has concluded that this agreement is within the scope of ASC 605-25, *Revenue Recognition, Multiple-Element Arrangements*. Pursuant to this guidance, the Company identified the following deliverables: (i) licenses, (ii) clinical supply and manufacturing obligations, (iii) rights to access and use materials and data, and (iv) rights to additional intellectual property. All other potential deliverables included in the arrangement have been deemed either contingent or inconsequential or perfunctory, individually and in the aggregate. Moreover, the Company has evaluated all deliverables included in the KHK License Agreement and determined that there are two units of accounting in connection with its obligations at inception under the KHK License Agreement: (i) license unit of accounting and (ii) rights to additional intellectual property. The first three deliverables identified above comprise the license unit of accounting. The Company concluded that the stand-alone selling price for the rights to additional intellectual property unit of account is immaterial. As such, the entire $17.3 million allocated to the upfront payment was allocated to the license unit of accounting.

The arrangement consideration allocated to the license unit of accounting will be recognized as revenue ratably over the Company's expected services period (currently expected to be through 2029) commencing on the date of the first delivery of the clinical trial materials. In June 2015, the Company began delivering clinical materials to KHK and commenced recognizing revenue from the upfront consideration of $17.3 million. During the years ended December 31, 2016 and 2015, the Company recognized $1.2 million and $0.6 million, respectively, of revenue associated with the KHK License Agreement. As of December 31, 2016, there was $15.4 million of deferred revenue related to the KHK License Agreement, which is classified as current or long-term in the consolidated balance sheets.

In October 2016, the Company entered into a clinical trial co-funding agreement with KHK under which the Company will expand 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 $695,000 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. During the second quarter of 2016, the ECOG Agreement was amended to provide additional study activities and the contractual obligation increased by $0.8 million. As of December 31, 2016, the Company's aggregate payment obligations under this agreement were approximately $21.4 million; and as of December 31, 2016, the Company's remaining payment obligations are approximately $12.9 million over an estimated period of approximately four years. During the first quarter of 2017, the ECOG Agreement was amended to expand the study to include enrollments from sites in Korea and the contractual obligation increased by $0.5 million.

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 is exercised or the closing of the IPO. Upon the closing of the IPO, the total number of shares of the Company's common stock issuable upon exercise of the warrant was set at 357,840. Prior to 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, which requires 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 is exercisable at an exercise price of $1.54 per share and expires 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 on March 8, 2016, using current assumptions just prior to the reclassification.

The total shares exercisable under the warrant, the fair value associated with the warrant and the Black-Scholes option-pricing model assumptions used to value the shares of common stock issuable pursuant to the warrant were as follows:

	Total Shares of Common Stock Issuable Under the Warrant	Average Exercise Price	Fair Value of Common Stock	Estimated Volatility	Risk-Free Interest Rate	Estimated Dividend Yield	Estimated Remaining Contractual Life (in years)	Fair Value of Warrant Liability
March 8, 2016	357,840	$ 1.54	$ 13.55	69%	1.82%	0.0%	10.00	$ 4,551
December 31, 2015	277,486	$ 1.54	$ 11.13	73%	2.15%	0.0%	8.06	$ 2,848

6. Property and Equipment, net

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

	December 31,	
	2016	2015
Office and computer equipment	$ 117	$ 117
Furniture and fixtures	195	74
Office equipment under capital lease	13	13
Leasehold improvements	215	48
Construction in progress	—	28
Total property and equipment	540	280
Accumulated depreciation	(280)	(192)
Property and equipment, net	$ 260	$ 88

7. 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, 2016, 2015 and 2014.

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

		Fair Value Measurements Using		
	Total Carrying Value	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
December 31, 2016				
Assets:				
Cash equivalents	$ 23,844	$17,089	$ 6,755	$ —
Short-term investments	81,486	—	81,486	—
Total assets	$105,330	$17,089	$ 88,241	$ —
December 31, 2015				
Assets:				
Cash equivalents	$ 23,154	$ 9,208	$ 13,946	$ —
Short-term investments	63,310	—	63,310	—
Total assets	$ 86,464	$ 9,208	$ 77,256	$ —
Liabilities:				
Derivative liability	$ 133	$ —	$ —	$ 133
Common stock warrant liability	2,848	—	—	2,848
Total liabilities	$ 2,981	$ —	$ —	$ 2,981

Cash equivalents of $17.1 million as of December 31, 2016 and $9.2 million as of December 31, 2015 consisted of overnight investments, money market funds and highly rated corporate bonds 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 $6.8 million as of December 31, 2016 and $13.9 million as of December 31, 2015 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 $81.5 million as of December 31, 2016 and $63.3 million as of December 31, 2015 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 investments are classified as available-for-sale securities. As of December 31, 2016, the remaining contractual maturities of the available-for-sale securities were less than one year, 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, 2016. 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, 2016, 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, 2016				
Commercial paper	$ 30,125	$ 61	$ —	$30,186
Corporate bonds	51,305	6	(11)	51,300
	$ 81,430	$ 67	$ (11)	$81,486
December 31, 2015				
Commercial paper	$ 28,980	$ 48	$ —	$29,028
Corporate bonds	34,302	—	(20)	34,282
	$ 63,282	$ 48	$ (20)	$63,310

A roll-forward of the recurring fair value measurements of the common stock warrant liability and the derivative liability categorized with Level 3 inputs are as follows (in thousands):

	Common Stock Warrant Liability	Derivative Liability
Balance—January 1, 2014	$ 2,482	$ —
Initial fair value of derivative	—	130
Change in fair value	(1,789)	(4)
Balance—December 31, 2014	693	126
Change in fair value	2,155	7
Balance—December 31, 2015	2,848	133
Change in fair value	1,703	17
Reclassification	(4,551)	(150)
Balance—December 31, 2016	$ —	$ —

The common stock warrant liability was recorded at fair value determined by using the Black-Scholes option-pricing model. This method of valuation involves using inputs such as the fair value of the Company's common stock, stock price volatility, the contractual term of the warrant, risk-free interest rates, and dividend yields. Due to the nature of these inputs, the valuation of the warrant was considered a Level 3 measurement. Upon the closing of the IPO, the warrant was reclassified to additional paid-in capital. See Note 5 for further discussion of the accounting for the Bayer common stock warrant as well as for a summary of the significant inputs and assumptions used to determine the fair value of the warrant.

The derivative liability related to the contingent success fee owed under the term loans. Upon the completion of an IPO or upon the occurrence of certain change of control or liquidation events, the Company was required to pay a $0.2 million success fee. The Company had recorded the success fee as a derivative financial liability. The initial fair value of the derivative of $0.1 million had been recorded as a debt discount. The term loans were paid in full in October 2015; however, the liability for the success fee survived the repayment of the term loans. Upon completion of the IPO this is no longer accounted for as a derivative, and the success fee of $0.2 million that is payable by June 2018 is included in other long-term liabilities.

8. Prepaid Expenses and Other Current Assets

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

	December 31,	
	2016	2015
Short-term deposits	$1,630	$ 805
Prepaid clinical supplies	461	210
Interest receivable on short-term investments	306	258
Reimbursable costs	262	2
Prepaid insurance	168	54
Other	202	135
Total prepaid expenses and other current assets	$3,029	$1,464

9. Accrued Expenses and Other Current Liabilities

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

	December 31,	
	2016	2015
Accrued professional fees	$ 247	$ 561
Accrued compensation and related costs	1,641	698
Accrued clinical costs	4,493	574
Derivative liability	—	133
Other	390	209
Total accrued expenses	$6,771	$2,175

10. Convertible Notes

In September 2014, the Company entered into a bridge loan financing with various investors, in which it issued convertible unsecured promissory notes for an aggregate principal amount of $5.0 million (the “2014 Notes”), in two closings. The first closing occurred in September 2014 and $4.9 million was received, and the balance of $0.1 million was received in October 2014. The 2014 Notes accrued interest at 6% per annum and had a maturity date of September 30, 2015 (the “Maturity Date”). The 2014 Notes were convertible upon the occurrence of the certain events during the period that the loans are outstanding. In June 2015, in conjunction with the Series C-1 financing, the outstanding principal of $5.0 million of the 2014 Notes and the related accrued interest of $0.2 million were converted into 372,446 shares of Series C-1 at $14.00 per share, which was the same price paid by Series C-1 investors.

11. Long-Term Debt

Solar Capital, Ltd, Term Loan

In June 2014, the Company entered into a loan and security agreement with Solar Capital Ltd. (“Solar”), as collateral agent and lender, consisting of a $15.0 million senior secured term loan facility. The loan was secured by substantially all of the Company’s existing and after-acquired assets except its intellectual property, but including right of payment with respect to any such intellectual property and all proceeds from the disposition of any such intellectual property. The intellectual property of the Company was subject to a negative pledge. In September and December 2014, the Company amended the term loan facility. The term loan facility had a maturity date of June 13, 2018.

In September 2014, the initial term loan (the “Term A Loan”), in the aggregate principal amount of $5.0 million was funded; and in December 2014, a second term loan (the “Term C Loan”) in the aggregate principal amount of $4.0 million was funded with the following post-closing conditions: pursuant to the KHK License Agreement, the Company was required to receive $7.5 million in net equity proceeds no later than January 9, 2015 and was required to receive $17.5 million in license-related proceeds no later than February 13, 2015, or return the $4.0 million of proceeds from Term Loan C to Solar. The Company achieved the post-closing conditions.

Interest accrued at a floating rate per annum equal to LIBOR plus 8.8%, payable monthly in arrears. The Company was required to make interest-only payments on any term loans funded under the term loan facility until July 1, 2015. Beginning on July 1, 2015, it was required to make payments of principal plus accrued interest in equal monthly installments until the maturity date. In addition, the Company was required to pay a final fee equal to 4% of the amount of term loans funded that was due on the earlier of the maturity date of the term loan facility or upon the occurrence of certain change of control or liquidity events. The Company accrued the final fee of $0.4 million on the outstanding term loans through interest expense using the effective-interest method over the period that the debt was outstanding. The Company incurred $0.3 million of debt issuance costs for this term loan facility, which were amortized as interest expense over the period that the related debt was outstanding.

The Company had the option to prepay the term loans provided it paid a prepayment fee equal to 2% of the outstanding principal if paid prior to the one-year anniversary and 1% of the outstanding principal if paid after the one-year anniversary of the funding. In October 2015, the Company prepaid the outstanding balance on the term loans of $8.3 million plus accrued interest of $0.1 million and a final fee and prepayment penalty of $0.4 million. In conjunction with this prepayment, the Company recorded an expense of $0.3 million for the final fee and prepayment penalty and wrote off $0.3 million of unamortized debt discount and deferred issuance costs related to the term loans.

Upon the completion of an IPO or upon the occurrence of certain change of control or liquidity events, the Company is required to pay a $0.2 million success fee that will be due on the earlier of the maturity date of the term loan facility or upon the occurrence of certain change of control or liquidity events. The Company initially recorded the success fee as a derivative financial liability. The initial fair value of the derivative of $0.1 million was recorded as a debt discount. The term loans were paid in full in October 2015; however, the liability for the success fee survived the repayment of the term loans. Upon completion of the IPO, the success fee is no longer considered a derivative liability. The success fee of $0.2 million is payable by June 2018 and included in other long-term liabilities.

12. Convertible Preferred Stock

Upon the closing of the IPO, all of the outstanding shares of the Company’s convertible preferred stock were converted into 12,872,551 shares of its common stock. As of December 31, 2016, the Company does not have any convertible preferred stock issued or outstanding. 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 now authorized to issue 10,000,000 shares of preferred stock in one or more series and to fix the powers, designations, preferences and relative participating option or other rights thereof, including dividend rights, conversion rights, voting rights, redemption terms, liquidation preferences and the number of shares constituting any series, without any further vote or action by the Company’s shareholders.

Convertible preferred stock consisted of the following (in thousands, except share data) as of December 31, 2015:

	Preferred Shares Designated	Issuance Date	Preferred Shares Issued and Outstanding	Liquidation Preference	Carrying Value
Series A-1	3,160,975	March 2013	2,801,745	$ 48,032	$ 65,666
Series B	3,382,113	March and August 2013	272,240	2,933	5,084
Series B-1	3,965,411	March, April, July, August and November 2013 and January 2015	3,568,020	96,348	96,348
Series C-1	6,090,481	June and August 2015	6,090,461	152,015	152,015
Total					$319,113
Series A	3,512,194	March and August 2013	700,435	$ —	$ 7,231

In August 2015, the Company issued 4,377,902 additional shares of Series C-1 for $61.1 million in cash, net of offering costs of $0.2 million. On the date of issuance, the Company recorded accretion of $46.1 million to record the convertible preferred stock at its redemption value.

In June 2015, the Company issued 1,712,559 shares of Series C-1 for $18.5 million in cash, net of offering costs of $0.2 million, and the conversion of the outstanding principal on the 2014 Notes of $5.0 million and related accrued interest of $0.2 million. On the date of issuance, the Company recorded accretion of $18.2 million to record the convertible preferred stock at its redemption value.

In January 2015, in accordance with the terms of the KHK License Agreement, the Company issued 536,049 shares of Series B-1 at an issuance price of $14.39 per share, the fair value of the Series B-1 based on the results of a contemporaneous valuation. On the date of issuance, the Company recorded accretion of $5.4 million to record the convertible preferred stock at its redemption value.

13. 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 now 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.

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

	December 31, 2016
Common stock issuable under Bayer warrant	357,840
Options to purchase common stock	4,025,966
Restricted stock subject to future vesting	8,542
Employee Stock Purchase Plan	250,000
Total	4,642,348

14. 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 replaces 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, 2016, there were 1,465,229 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, 2017, the shares available for issuance under the 2015 Plan were increased to 4,754,914.

Stock Options

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

	Years Ended December 31,		
	2016	2015	2014
Research and development	$ 919	$ 846	$ 527
General and administrative	3,789	3,036	1,730
Total	$4,708	$3,882	$2,257

As of December 31, 2016, there was $7.8 million of unrecognized compensation cost related to employee and non-employee unvested stock options and unvested restricted stock granted under the 2007 and 2015 Plans, which is expected to be recognized over a weighted-average remaining service period of 2.5 years. Stock compensation costs have not been capitalized by the Company.

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 service-based 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 accounting guidance for stock-based compensation requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. 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,		
	2016	2015	2014
Expected term (in years)	5.85	5.89	5.96
Volatility rate	71.40%	69.92%	70.36%
Risk-free interest rate	1.41%	1.73%	1.91%
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 our IPO, the fair value of the common stock underlying the stock options has been 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, 2016	2,606,195	$ 7.56	8.3	$ 9,463
Granted	478,530	$ 12.64		
Exercised	(441,573)	$ 4.66		
Canceled or forfeited	(82,415)	$ 8.87		
Outstanding—December 31, 2016	2,560,737	$ 8.97	8.4	$ 503
Exercisable—December 31, 2016	2,234,249	$ 8.33	8.2	$ 503
Options vested, exercisable or expected to vest—December 31, 2016	2,503,957	$ 8.94	8.5	$ 504

The weighted-average grant date fair value of options granted during the years ended December 31, 2016, 2015 and 2014, was $7.94, $5.74 and $8.92, 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 441,573 options exercised for the year ended December 31, 2016, resulting in total proceeds of $2.1 million; and 41,607 options exercised for the year ended December 31, 2015, resulting in total proceeds of $0.2 million, including 16,731 shares subject to repurchase by the Company. No options were exercised in 2014. The intrinsic value of options exercised during the years ended December 31, 2016 and 2015 was $3.8 million, and $0.2 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.

The 2007 Plan allowed employees to exercise unvested options in exchange for restricted common stock. Such arrangements permitted the Company to subsequently repurchase such shares at the exercise price if the vesting conditions were not satisfied. Such an exercise is not substantive for accounting purposes; therefore, the payment received by the Company for the exercise price is recognized as an early exercise liability on the Company's consolidated balance sheet and will be transferred to common stock and additional paid-in capital as such shares vest. The Company issued 16,731 shares of restricted common stock upon early exercise of stock options during the year ended December 31, 2015, with total proceeds of $0.1 million on the exercise date. As of December 31, 2016, 8,542 unvested shares were legally issued and outstanding and subject to repurchase by the Company. In connection with these unvested shares, the Company has recorded a liability of $0.1 million, of which $42,000 is included in accrued expenses and other current liabilities and $17,000 is included in other long-term liabilities in the Company's consolidated balance sheet.

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 our 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. No offering periods have been approved at this time; and as of the December 31, 2016, no shares of common stock have been purchased under the ESPP.

Effective January 1, 2017, and continuing until the expiration of the ESPP, which is the earlier of (a) ten years after the date of adoption of the ESPP or (b) such time as all shares of common stock that may be made available for purchase under the ESPP have been issued, the number of common shares available for purchase by the Company's employees will automatically increase annually on January 1, beginning January 1, 2017, in an amount equal to the lesser of (i) 1% of the total number of issued and outstanding common stock as December 31 of the immediately preceding year or (ii) 250,000 shares of our common stock or such lesser number of shares as determined by the Company's board of directors. On January 1, 2017, the shares of common stock reserved for issuance under the ESPP was increased to 432,237.

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, 2016, 2015 and 2014, the Company made $72,000, $33,000 and $0 contributions to the plan, respectively.

15. 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 net 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,	
	2016	2015
Deferred tax assets (liabilities):		
Net operating loss carryforwards	$ 13,744	$ 14,598
Research and development credits	1,739	1,452
Capitalized start-up and research and development costs	47,048	37,641
Deferred revenue	5,420	—
Depreciation and amortization	(10,530)	(8,433)
Accruals	604	332
Other temporary differences	2,298	1,769
Deferred tax assets before valuation allowance	60,323	47,359
Valuation allowances	(60,323)	(47,359)
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 increased by $13.0 million and $6.6 million in 2016 and 2015, respectively, due to the increase in deferred tax assets, primarily due to increases in capitalized start-up and research and development costs.

As of December 31, 2016, the Company had approximately $36.0 million and $27.5 million in federal and state Net Operating Losses ("NOLs"), respectively, which expire at various dates through 2036. As of December 31, 2016, the Company had federal and state research credits of $1.1 million and $0.9 million, respectively, which begin to expire in 2021.

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, have limited and 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 March 8, 2016 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 our stock ownership, some of which may be outside the Company's control. As a result, the Company's 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 the Company. 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, 2016 and 2015, 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, 2016, 2015 and 2014. 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, 2016, 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,		
	2016	2015	2014
Unrecognized tax benefit—beginning of year	$241	$241	$ 680
Decreases related to prior period positions	—	—	(439)
Unrecognized tax benefit—end of year	$241	$241	$ 241

The Company files tax returns in the United States, Massachusetts, California, South Carolina, 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.

16. 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 new five-year operating lease for approximately 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 Company's existing Waltham lease expires in April 2017 and will relocate to the new space on March 1, 2017. 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 will record 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 new 62-month building lease for approximately 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 also has an option to cancel the lease after three years with the termination fee consisting of three months of rent. 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.

In December 2013, the Company entered into a 40-month lease for approximately 4,712 square feet of office space in Waltham, Massachusetts. 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, 2016, are as follows (in thousands):

	Operating Leases	Capital Lease Obligations
For the years ended December 31,		
2017	$ 396	$ 4
2018	524	3
2019	569	—
2020	588	—
2021	395	—
2022 and thereafter	59	—
Total minimum lease payments	$ 2,531	7
Less amounts representing interest		1
Present value of net minimum lease payments		$ 6

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 $0.4 million, $0.1 million and $0.1 million for the years ended December 31, 2016, 2015, and 2014, respectively.

17. Supplemental Cash Flow Information

	Years Ended December 31,		
	2016	2015	2014
		(In thousands)	
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:			
Interest paid	$ 2	$ 688	$ 170
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING ACTIVITIES:			
Accretion of convertible preferred stock to redemption value	$ —	$69,715	$ —
Accretion of dividends on convertible preferred stock	$ 2,598	$10,011	$6,529
Conversion of convertible notes and accrued interest into Series C-1 convertible preferred stock	$ —	$ 5,211	$ —
Term loan proceeds allocated to derivative liability	$ —	$ —	$ 130
Issuance costs included in accounts payable and accrued expenses	$ —	$ 376	$ 614
Property and equipment purchases included in accrued expenses	$ —	$ 27	$ 3
Vesting of restricted stock	$ 42	$ 14	$ —
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	$ —	$ —

18. 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.

In June 2015, in conjunction with the Series C-1 financing, the Company issued 1,130,740 shares of Series C-1 convertible preferred stock for total gross proceeds, including 2014 Notes conversion and cash purchase price, of $12.7 million to existing stockholders of the Company; and in August 2015 in conjunction with the Series C-1 financing, the Company issued 474,628 shares of Series C-1 convertible preferred stock for total gross proceeds of $5.3 million to an existing stockholder of the Company. See Note 12 for further discussion.

In September 2014, the Company issued $5.0 million of 2014 Notes to stockholders of the Company. In June 2015, in conjunction with the Series C-1 financing, the outstanding principal of $5.0 million and the related accrued interest of $0.2 million on the 2014 Notes were converted into 465,563 shares of Series C-1. As of December 31, 2015, no amount of principal or related accrued interest on the 2014 Notes was outstanding. As of December 31, 2014, an aggregate of $5.0 million of principal was outstanding under the 2014 Notes and $0.1 million of related accrued interest were held by stockholders of the Company. Interest expense related to the 2014 Notes held by these stockholders was $0.3 million and $0.1 million for the years ended December 31, 2015 and 2014, respectively.

19. Quarterly financial information (unaudited)

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

	Three Months Ended 2016			
In thousands, except per share data	March 31	June 30	September 30	December 31
License fees	$ 305	$ 305	$ 305	$ 305
Operating expenses:				
Research and development(1)	4,786	6,131	12,274	8,474
General and administrative	4,272	2,808	3,269	2,972
Total expenses	9,058	8,939	15,543	11,446
Loss from operations	(8,753)	(8,634)	(15,238)	(11,141)
Other (expense) income	(1,577)	276	269	326
Net loss	$ (10,330)	$ (8,358)	$ (14,969)	$ (10,815)
Net loss per share attributable to common stockholders —basic and diluted	$ (2.85)	$ (0.47)	$ (0.84)	$ (0.59)
Weighted-average shares—basic and diluted	4,541,536	17,769,514	17,899,481	18,193,027

	Three Months Ended 2015			
In thousands, except per share data	March 31	June 30	September 30	December 31
License fees	$ —	$ 17	$ 305	$ 305
Operating expenses:				
Research and development	1,723	2,271	2,968	2,587
General and administrative	2,711	3,288	3,195	2,397
Total expenses	4,434	5,559	6,163	4,984
Loss from operations	(4,434)	(5,542)	(5,858)	(4,679)
Other (expense) income	(477)	(672)	(1,873)	(584)
Net loss	$ (4,911)	$ (6,214)	$ (7,731)	$ (5,263)
Net loss per share attributable to common stockholders —basic and diluted	$ (206.30)	$ (440.52)	$ (790.85)	$ (105.57)
Weighted-average shares—basic and diluted	58,517	59,788	71,639	83,157

(1) Research and development expenses for three months ended September 30, 2016 included the $5.0 million upfront payment related to the UCB License Agreement.

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EXHIBIT INDEX

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 3.1 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).
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).
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).

Exhibit No.	Description
10.11*	2015 Omnibus Incentive Plan (incorporated herein by reference to Exhibit 10.1 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*	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).
10.19†	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).
10.20†	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).
10.21	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).
10.22†	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).
10.23†	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).

Exhibit No.	Description
10.24†	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).
10.25†	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).
10.26†	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).
10.27†	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).
10.28†	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).
10.29†	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).
10.30†	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).
10.32	Loan and Security Agreement by and among the company, Solar Capital Ltd. and the Lenders listed therein, dated as of June 13, 2014 (incorporated herein by reference to Exhibit 10.29 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016).
10.33	First Amendment to Loan and Security Agreement by and among the company, Solar Capital Ltd. and the Lenders listed therein, dated as of September 25, 2014 (incorporated herein by reference to Exhibit 10.30 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016).
10.34	Second Amendment to Loan and Security Agreement by and among the company, Solar Capital Ltd. and the Lenders listed therein, dated as of December 31, 2014 (incorporated herein by reference to Exhibit 10.31 to the Company's Registration Statement on Form S-1 (File No. 333-208861), as filed with the SEC on January 4, 2016).
10.35†	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).
10.36†	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).

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Exhibit No.	Description
10.37†	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).
10.38†	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).
10.39†	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).
10.40†	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).
10.41†	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).
10.42†	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).
10.43	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).
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.

EXHIBIT 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in Registration Statement No. 333-210412 on Form S-8 of our report dated March 14, 2017, relating to the financial statements of Syndax Pharmaceuticals, Inc. and its subsidiaries appearing in this Annual Report on Form 10-K of Syndax Pharmaceuticals, Inc. for the year ended December 31, 2016.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
March 14, 2017

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

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; 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 14, 2017

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

(c) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; 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 14, 2017

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, 2016, 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 14, 2017

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

Date: March 14, 2017

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