Filed Pursuant to Rule 424(b)(4)
Registration No. 333-208861

PROSPECTUS

4,400,000 Shares

Common Stock

This is the initial public offering of shares of common stock of Syndax Pharmaceuticals, Inc. We are offering 4,400,000 shares of our common stock. Prior to this offering, there has been no public market for our common stock. The initial public offering price is $12.00 per share. Our common stock has been approved for listing on the NASDAQ Global Select Market under the symbol "SNDX."

We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 10 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Initial public offering price	$ 12.00	$52,800,000
Underwriting discounts and commissions(1)	$ 0.84	$ 3,696,000
Proceeds, before expenses, to us	$ 11.16	$49,104,000

(1) See "Underwriting" for a description of the compensation payable to the underwriters.

Delivery of the shares of common stock purchased in this offering is expected to be made on or about March 8, 2016. We have granted the underwriters an option for a period of 30 days to purchase up to 660,000 additional shares of common stock solely to cover over-allotments, if any.

Morgan Stanley **Citigroup**

JMP Securities **Oppenheimer & Co.**

Prospectus dated March 2, 2016

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You should rely only on the information contained in this prospectus and any free writing prospectus prepared by or on behalf of us or to which we have referred you. We have not authorized anyone to provide you with information that is different. We are offering to sell shares of our common stock, and seeking offers to buy shares of our common stock, only in jurisdictions where offers and sales are permitted. The information in this prospectus is complete and accurate only as of the date on the front cover of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock.

Until and including March 27, 2016 (25 days after the date of this prospectus), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of shares of our common stock and the distribution of this prospectus outside the United States.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to "Syndax," "the company," "we," "us," "our" and similar references refer to Syndax Pharmaceuticals, Inc. and our wholly owned subsidiary. "Syndax" is a registered trademark and the "Syndax" and "Syndax Pharmaceuticals" logos are unregistered trademarks of the company. This prospectus also contains registered marks, trademarks and trade names of other companies. All other trademarks, registered marks and trade names appearing in this prospectus are the property of their respective holders.

PROSPECTUS SUMMARY

The following summary highlights information contained elsewhere in this prospectus and is qualified in its entirety by the more detailed information and consolidated financial statements and related notes thereto included elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. Before you decide to invest in our common stock, you should read and carefully consider the following summary together with the entire prospectus, including our consolidated financial statements and the related notes thereto included elsewhere in this prospectus and the matters discussed in the sections titled "Risk Factors," "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Some of the statements in this prospectus constitute forward-looking statements that involve risks and uncertainties. See the section titled "Special Note Regarding Forward-Looking Statements and Industry Data." Our actual results could differ materially from those anticipated in such forward-looking statements as a result of certain factors, including those discussed in the section titled "Risk Factors" and other sections of this prospectus.

Our Company

We are a clinical stage biopharmaceutical company developing entinostat as a combination therapy in multiple cancer indications with our initial focus on tumors that have shown sensitivity to immunotherapy, including lung cancer, melanoma, ovarian cancer and triple negative breast cancer, or TNBC. Entinostat is our oral, small molecule drug 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 900 cancer patients. We are currently evaluating entinostat in combination with *Keytruda*® (pembrolizumab) in a Phase 1b/2 clinical trial for non-small cell lung cancer, or NSCLC, and melanoma, and we plan to initiate a Phase 1b/2 clinical trial for entinostat in combination with atezolizumab in TNBC in the first half of 2016 and a Phase 1b/2 clinical trial for entinostat in combination with avelumab in ovarian cancer in the second half of 2016. 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.

We are also developing entinostat for use in advanced hormone receptor positive, or HR+, breast cancer. Following positive results from our Phase 2b clinical trial, ENCORE 301, entinostat in combination with *Aromasin*® (exemestane tablets) was granted breakthrough therapy designation by the U.S. Food and Drug Administration, or the FDA, in advanced HR+ breast cancer for which it is currently being evaluated in a Phase 3 clinical trial.

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 PDL-1, 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 PDL-1 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. We believe entinostat's well-characterized safety profile and mechanism of action allows it to be readily combined with, and thereby enhance the activity of, conventional and novel cancer therapies, such as immune checkpoint inhibitors, hormone therapies and chemotherapies.

Entinostat is currently being studied in clinical trials across a broad range of solid tumors, including breast cancer, NSCLC, renal cell carcinoma and ovarian cancer. We are working in collaboration with Merck & Co. Inc., or Merck, to study the combination of entinostat with Merck's immune checkpoint inhibitor, *Keytruda*, in a Phase 1b/2 clinical trial, ENCORE 601, of up to 178 patients with NSCLC or melanoma. Patient enrollment was initiated in the Phase 1b portion of the clinical trial in August 2015, which will evaluate the safety and tolerability of the combination of entinostat and *Keytruda*, and the Phase 2 portion of the clinical trial will assess the efficacy of entinostat combined with *Keytruda* in patients with either NSCLC or melanoma. 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 investigational immune checkpoint inhibitor, atezolizumab, in a Phase 1b/2 clinical trial, ENCORE 602, of patients with TNBC. We have also entered into a collaboration with Ares Trading S.A., a subsidiary of Merck KGaA, Darmstadt, Germany, or Merck KGaA, and Pfizer Inc. to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with an investigational monoclonal antibody targeting PDL-1, 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-PDL-1 IgG1 monoclonal antibody (MSB0010718C). Additionally, entinostat is being evaluated in two ongoing and one 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.

We are also providing financial and operational support for an ongoing Phase 3 clinical trial in advanced HR+ breast cancer in combination with *Aromasin.* Eastern Cooperative Oncology Group-American College of Radiology Imaging Network Cancer Research Group, or ECOG-ACRIN, is conducting this clinical trial under sponsorship and funding support from the National Cancer Institute,

or NCI. The Phase 3 clinical trial 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.

Clinical Development Programs of Entinostat

The following table sets forth information pertaining to the clinical trials for entinostat with our initial focus on advancing ENCORE 601, ENCORE 602 and ENCORE 603 in immuno-oncology and E2112, our collaboration with ECOG-ACRIN and the NCI, in advanced HR+ breast cancer.

Immuno-Oncology	Preclinical	Phase 1	Phase 2	Phase 3	Indication	Sponsor	Data Expected
ENCORE 601: Entinostat + *Keytruda*					NSCLC / Melanoma	Syndax	First half of 2016
ENCORE 602: Entinostat + atezolizumab					TNBC	Syndax	Second half of 2016
ENCORE 603: Entinostat + avelumab					Ovarian Cancer	Syndax	First half of 2017
J1353: Epigenetic Priming to Immunotherapy					NSCLC	Johns Hopkins	Second half of 2016
NCI-7870: Entinostat + *Proleukin*					Renal cell carcinoma	NCI	January 2016
NCI-9844: Entinostat + *Opdivo* + *Yervoy*					Solid tumors	NCI	Second half of 2017
Advanced HR+ Breast Cancer	Preclinical	Phase 1	Phase 2	Phase 3	Indication	Sponsor	Data Expected
E2112: Entinostat + *Aromasin*					Advanced HR+, HER2- breast cancer	NCI/Syndax	No sooner than second half of 2017 (PFS) 2019 (OS)
Other Indications	Preclinical	Phase 1	Phase 2	Phase 3	Indication	Sponsor	Data Expected /Received
NCI-8871: Entinostat + *Tykerb* + *Herceptin*					HER2+ breast cancer	NCI	December 2015
NCI-9253: Epigenetic Priming to Chemotherapy					NSCLC	NCI	Second half of 2017

Our Strategy

We are focused on 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 PDL-1 inhibitors;
- pursue regulatory approval of entinostat in indications with significant unmet need and commercial potential;
- continue to develop and obtain regulatory approval for entinostat in combination with hormone therapy in advanced HR+ breast cancer; and
- 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.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks and uncertainties. As a late-stage biopharmaceutical company, we face many risks inherent in our business and our industry generally. You should carefully consider all of the information set forth in this prospectus and, in particular, the information in the section titled "Risk Factors," prior to making an investment in our common stock. These risks include, among others, the following:

- We have no source of product revenue, may never achieve or maintain profitability, have incurred net losses since our inception and anticipate that we will continue to incur net losses for the foreseeable future.
- We will require additional capital to finance our planned operations, which may not be available to us on acceptable terms, or at all.
- Entinostat currently is our only product candidate. If we are unable to successfully complete clinical development of, obtain regulatory approval for and commercialize entinostat, our business prospects will be significantly harmed.
- 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.
- 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 are dependent on Merck, Genentech, Merck KGaA and Pfizer and any future collaborators to perform satisfactorily under our agreements.
- 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 entinostat could harm our business.
- We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.
- If we are unable to obtain or protect intellectual property rights, we may not be able to compete effectively in our market.
- If we breach our license agreement with Bayer Pharma AG (formerly known as Bayer Schering Pharma AG) 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 Corporate Information

We were incorporated under the laws of the State of Delaware in October 2005. Our principal executive offices are located at 400 Totten Pond Road, Suite 110, Waltham, Massachusetts 02451, and our telephone number is (781) 419-1400. Our website address is www.syndax.com. Our website and the information contained on, or that can be accessed through, the website will not be deemed to be incorporated by reference in, and are not considered part of, this prospectus. You should not rely on any such information in making your decision to purchase our common stock.

Implications of Being an Emerging Growth Company

As a company with less than $1.0 billion in revenue during our last fiscal year, we qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. An emerging growth company may take advantage of specified reduced reporting and other burdens that are otherwise applicable generally to public companies. These provisions include:

- a requirement to have only two years of audited financial statements and only two years of related management's discussion and analysis in this prospectus;
- an exemption from compliance with the auditor attestation requirement on the effectiveness of our internal control over financial reporting;
- an exemption from compliance with any requirement that the Public Company Accounting Oversight Board may adopt regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure about the company's executive compensation arrangements; and
- exemptions from the requirements to obtain a non-binding advisory vote on executive compensation or a stockholder approval of any golden parachute arrangements.

We may take advantage of these provisions 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, have more than $700 million in market value of our capital stock held by non-affiliates, or issue more than $1.0 billion of non-convertible debt over a three-year period. We may choose to take advantage of some, but not all, of the available benefits under the JOBS Act. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not emerging growth companies.

The Offering

Common stock to be offered by us	4,400,000 shares
Common stock to be outstanding immediately following this offering	17,372,675 shares
Over-allotment option	We have granted the underwriters an option for 30 days from the date of this prospectus to purchase up to 660,000 additional shares of common stock to cover over-allotments, if any.
Use of proceeds	We expect to use the proceeds from this offering for the following purposes: (i) to support the clinical trials of entinostat in combination with Keytruda® (pembrolizumab), atezolizumab and avelumab; (ii) to support additional clinical trials of entinostat in combination with immune checkpoint inhibitors; (iii) to support the Phase 3 clinical trial of entinostat in advanced HR+ breast cancer; (iv) to conduct activities to support the filing of a New Drug Application for entinostat, including manufacturing of registration batches of active pharmaceutical ingredient and final drug product; and (v) the remainder for working capital and general corporate purposes. See the section titled “Use of Proceeds” for a more complete description of the intended use of proceeds from this offering.
Risk factors	You should read the section of this prospectus titled “Risk Factors” for a discussion of factors to carefully consider before deciding to invest in shares of our common stock.
NASDAQ Global Select Market symbol	SNDX

The number of shares of our common stock outstanding immediately following this offering set forth above is based on 12,972,675 shares of our common stock outstanding as of December 31, 2015 (including 14,684 shares of unvested restricted stock subject to repurchase by us), which gives effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 12,872,551 shares of our common stock upon completion of this offering.

The number of shares of our common stock outstanding immediately following this offering excludes:

- 2,606,195 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2015 under our 2007 Stock Plan, as amended, or 2007 Plan, at a weighted-average exercise price of $7.56 per share;

- 355,857 shares of our common stock issuable upon the exercise of a warrant issued to Bayer on March 26, 2007, or the Bayer Warrant, at an exercise price of $1.54 per share, based upon 19,978,870 shares of our common stock outstanding as of December 31, 2015 on a fully diluted basis immediately following this offering, which warrant is expected to remain outstanding upon completion of this offering;
- 1,750,000 shares of our common stock reserved for issuance under our 2015 Omnibus Incentive Plan, or 2015 Plan, which will become effective upon completion of this offering, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2015 Plan; and
- 250,000 shares of our common stock reserved for issuance under our 2015 Employee Stock Purchase Plan, or ESPP, which will become effective upon completion of this offering, as well as any future increases in the number of shares of our common stock reserved for issuance under the ESPP.

Except as otherwise indicated, the information in this prospectus assumes or gives effect to:

- no exercise by the underwriters of their over-allotment option to purchase up to 660,000 additional shares of common stock from us;
- the conversion of all outstanding shares of our convertible preferred stock outstanding as of December 31, 2015 into an aggregate of 12,872,551 shares of our common stock upon completion of this offering;
- a 1-for-1.25 reverse stock split of our common stock and convertible preferred stock effected on February 24, 2016; and
- the filing of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur upon the completion of this offering.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following table summarizes our consolidated financial data. We have derived the following consolidated statements of operations data for the years ended December 31, 2014 and 2015 from our audited consolidated financial statements, included elsewhere in this prospectus. Our historical results are not necessarily indicative of results to be expected for any period in the future. The summary consolidated financial data presented below should be read in conjunction with the section titled "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 prospectus. The summary consolidated financial data in this section is not intended to replace our consolidated financial statements and the related notes thereto.

(in thousands, except share and per share data)	Years Ended December 31, 2014	2015
Consolidated Statements of Operations Data:		
Revenues:		
License fees	$ —	$ 627
Total revenues	—	627
Operating expenses:		
Research and development	10,175	9,549
General and administrative	11,157	11,591
Total operating expenses	21,332	21,140
Loss from operations	(21,332)	(20,513)
Other income (expense):		
Interest income	10	161
Interest expense	(299)	(1,575)
Change in fair value of common stock warrant liability	1,789	(2,155)
Other income (expense), net	4	(37)
Total other income (expense)	1,504	(3,606)
Net loss	$(19,828)	$ (24,119)
Net loss attributable to common stockholders—basic and diluted[(1)]	$(26,357)	$ (103,845)
Net loss per share attributable to common stockholders—basic and diluted[(1)]	$(453.02)	$ (1,519.27)
Weighted-average common shares outstanding used to compute net loss per share attributable to common stockholders—basic and diluted[(1)]:	58,181	68,352
Pro forma net loss per share attributable to common stockholders—basic and diluted[(1)]		$ (2.28)
Pro forma weighted-average common shares outstanding used to compute net loss per share attributable to common stockholders, basic and diluted[(1)]		9,597,519

(1) See Note 2 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the weighted-average number of shares used in the computation of the per share amounts.

(in thousands)	As of December 31, 2015 Actual	Pro Forma[1]	Pro Forma As Adjusted[2]
Consolidated Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 86,489	$ 86,489	$ 134,039
Total assets	89,903	89,903	135,832
Convertible preferred stock	319,113	—	—
Accumulated deficit	(259,675)	(259,675)	(259,675)
Total stockholders' (deficit) equity	(252,415)	69,546	115,850

(1) The pro forma column in the consolidated balance sheet data above gives effect to the conversion of all outstanding shares of our convertible preferred stock outstanding as of December 31, 2015 into an aggregate of 12,872,551 shares of our common stock upon completion of this offering and the reclassification of the common stock warrant liability to additional paid-in capital.

(2) The pro forma as adjusted column in the consolidated balance sheet data above gives additional effect to the sale of 4,400,000 shares of common stock in this offering at an initial public offering price of $12.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, as if the sale of the shares in this offering had occurred as of December 31, 2015.

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before making your decision to invest in shares of our common stock, you should carefully consider the risks described below, together with the other information contained in this prospectus, including our consolidated financial statements and the related notes appearing at the end of this prospectus. We cannot assure you that any of the events discussed below will not occur. These events could harm our business, results of operations, financial condition and cash flows. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment.

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 years ended December 31, 2014 and 2015, we reported a net loss of $19.8 million and $24.1 million, respectively. As of December 31, 2015, we had an accumulated deficit of $259.7 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, entinostat. 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 entinostat. We do not anticipate generating revenue from the sale of entinostat for the foreseeable future. Our ability to generate future product revenue from entinostat 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, entinostat;
- launch, commercialize and achieve market acceptance of entinostat, and if launched independently, successfully establish a sales, marketing and distribution infrastructure;

- 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 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 the development of a new chemical entity, including that entinostat may not achieve the endpoints of applicable trials, 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 U.S. Food and Drug Administration, or 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 entinostat, 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 entinostat 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 the net proceeds from this offering, together with our existing cash and cash equivalents and short-term investments, will fund our projected operating expenses and capital expenditure requirements for at least the next 24 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 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. 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 entinostat 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 for entinostat;
- the outcome, timing and cost of seeking and obtaining regulatory approvals from the FDA and 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 entinostat;
- 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 entinostat if entinostat 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 become a public 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 September 30, 2015 and determined that on March 30, 2007 and August 21, 2015 ownership changes had occurred. We may have experienced an ownership change subsequent to September 30, 2015, and we may also experience ownership changes in the future as a result of this offering or subsequent 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 is currently our only product candidate. If we are unable to successfully complete clinical development of, obtain regulatory approval for and commercialize entinostat, our business prospects will be significantly harmed.

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

- timely commencement and completion of the planned Phase 1b/2 clinical trials of entinostat in combination with *Keytruda*® (pembrolizumab), atezolizumab and avelumab;
- timely patient enrollment and completion of the Phase 3 clinical trial in advanced hormone receptor, or HR+, breast cancer, which may be significantly slower than we currently anticipate and will depend substantially upon the satisfactory performance of the Eastern Cooperative Oncology Group—American College of Radiology Imaging Network Cancer Research Group, or ECOG-ACRIN, and the National Cancer Institute, or NCI, and other third-party contractors;
- 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 entinostat's safety and efficacy for its proposed indications and the timely receipt of necessary marketing approvals from the FDA and foreign regulatory authorities;
- achieving and maintaining compliance with all regulatory requirements applicable to entinostat;
- 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 to develop, validate and maintain a commercially viable manufacturing process that is compliant with current Good Manufacturing Practices, or cGMP;
- the availability of commercial supplies of therapeutics, including *Aromasin*® (exemestane tablets) 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;
- our ability to successfully commercialize entinostat 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.

If we fail to obtain regulatory approval for, or are unable to successfully commercialize, entinostat, we will have no other product candidates to rely on. In addition, 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 begun to clinically test our strategy of combining entinostat with immune checkpoint inhibitors, and therefore 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 Special Protocol Assessment, or SPA, agreement with the FDA relating to the pivotal Phase 3 clinical trial of entinostat for advanced HR+ breast cancer, this agreement does not guarantee any particular outcome with respect to regulatory review of the trial or any associated New Drug Application, or NDA, for entinostat.

The protocol for the pivotal Phase 3 trial of entinostat in combination with *Aromasin* in advanced HR+ 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 an NDA. The SPA is an agreement that a Phase 3 clinical trial's design, clinical endpoints, patient population and statistical analyses are sufficient to support the efficacy claim. Agreement on the SPA is not a guarantee of approval, and there is no assurance that the design of, or data collected from, the trial will be adequate to obtain the requisite regulatory approval. 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+ 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+ breast cancer patients. The trial will measure two primary endpoints of progression-free survival, or PFS, and overall survival. Based on information received from ECOG-ACRIN to date, PFS data is expected no sooner than the second half 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+ 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+ 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*® (fulvestrant) and *Ibrance* (palbociclib), 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+ 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+ 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+ breast cancer commenced in the second quarter of 2014, and ECOG-ACRIN expects to have PFS data from this trial no sooner than 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 entinostat versus other compounds in clinical development or commercially available;
- evolving standard of care in treating cancer patients with immune-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 Inc., or Genentech, Ares Trading S.A., or Merck KGaA, and Pfizer, Inc., or 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 Kyowa Hakko Kirin Co., Ltd., or 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 affect on the development of entinostat for development and commercialization in the United States and the rest of the world.

We may be required to relinquish important rights to and control over the development and commercialization of entinostat 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, in the future, 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 entinostat 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 entinostat or any other product candidate, and it is possible that we will never obtain regulatory approval for entinostat or any future product candidates.

Entinostat 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 entinostat is safe and effective;
- failure of clinical trials to meet the primary endpoints or level of statistical significance required for approval;
- failure to demonstrate that entinostat's clinical and other benefits outweigh any 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 entinostat to support the submission and filing of an NDA or other submission or to obtain regulatory approval;
- failure to obtain approval of the manufacturing and testing processes or facilities of third-party contract 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 for a more limited patient population than we request, may grant approval contingent on the performance of costly post-marketing trials, may impose a Risk Evaluation and Mitigation Strategy, or REMS, or foreign regulatory authorities may require the establishment or modification of a similar strategy that may, for instance, restrict distribution of entinostat and impose burdensome implementation requirements on us, or may approve it with a label that does not include the labeling claims necessary or desirable for the successful commercialization of entinostat, all of which could limit our ability to successfully commercialize our drug products.

We are not developing entinostat as a monotherapy. A shortage in the supply of Aromasin, Keytruda, atezolizumab 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+ 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+ 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.

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

Even if entinostat receives regulatory approval, it 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 of entinostat 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 entinostat. The degree of market acceptance of entinostat 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 entinostat is approved;
- acceptance of entinostat as a safe and effective treatment by physicians, clinics and patients;
- the potential and perceived advantages of entinostat 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 entinostat.

If entinostat is approved but does 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 entinostat, we intend to rely on third parties for commercial manufacturing and distribution of entinostat 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. While we expect to continue to depend on third-party contract 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 contract manufacturers for compliance with cGMPs and for manufacture of both active drug substances and finished drug products. Facilities used by our contract 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 contract 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 contract manufacturers are engaged with other companies to supply and/or manufacture materials or products for such companies, which also exposes our contract 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 contract manufacturers' facility. If the FDA or a foreign regulatory agency does not approve these facilities for the manufacture of entinostat, 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 entinostat, 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 necessarily increase the likelihood that entinostat will receive marketing approval.

We have received breakthrough therapy designation for entinostat. 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. Entinostat when used in combination with *Aromasin* received a breakthrough therapy designation from the FDA based on the overall survival results from our completed Phase 2b clinical trial in advanced HR+ breast cancer. The trial showed statistically significant improvements in PFS, the primary endpoint, and overall survival, 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 entinostat receives regulatory approval, it may still face future development and regulatory difficulties.

Even if we obtain regulatory approval for entinostat, it 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 entinostat, 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 contract 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 entinostat.

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.

Entinostat 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 entinostat 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+ 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 entinostat 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 entinostat receives 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, entinostat;
- regulatory authorities may withdraw approvals of entinostat;
- regulatory authorities may require additional warnings on the entinostat label;
- the FDA or other regulatory authorities may issue safety alerts, Dear Healthcare Provider letters, press releases or other communications containing warnings about entinostat;
- 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 entinostat 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 entinostat 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 entinostat outside the United States.

In order to market and sell entinostat 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 entinostat 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+ breast cancer. Our failure to obtain approval of entinostat by foreign regulatory authorities may negatively impact the commercial prospects of entinostat and our business prospects could decline. Also, if regulatory approval for entinostat 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 entinostat 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+ 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 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 entinostat relative to marketed products and product candidates in development by third parties;
- the time it takes for entinostat to complete clinical development and receive marketing approval;
- our ability to commercialize entinostat if it receives regulatory approval;
- the price of entinostat, 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 entinostat if it receives 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 entinostat, the availability and price of our competitors' products could limit the demand and the price we are able to charge for entinostat. We may not be able to implement our business plan if the acceptance of entinostat is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to entinostat, or if physicians switch to other new drug or biologic products or choose to reserve entinostat for use in limited circumstances.

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

The commercial success of entinostat will depend in part on public acceptance of the use of cancer immunotherapies. Adverse events in clinical trials of entinostat 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, entinostat 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 entinostat, it 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 Centers for Medicare and Medicaid Services' 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 entinostat 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 entinostat in that particular country. Adverse pricing limitations may hinder our ability to recoup our investment even if entinostat obtains marketing approval.

There can be no assurance that entinostat, if it is 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 entinostat profitably.

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

In order to market entinostat or any other 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 drug 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 drug candidate.

Current and future legislation may increase the difficulty and cost for us to commercialize entinostat 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, President Obama signed into law 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. 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.

Other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. For example, in August 2011, the President 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 2024. In January 2013, 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.

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 entinostat.

We face an inherent risk of product liability exposure related to the testing of entinostat 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 entinostat 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 entinostat;
- 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 entinostat, 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 future arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell 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;
- the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, and their implementing regulations, or 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, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, contractual damages, reputational harm, 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 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 the 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 2029. After expiry of RE39,754 in 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.

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 entinostat 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 result in our having 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 entinostat.

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 Leahy-Smith Act, was signed into law. The Leahy-Smith 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 Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith 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 Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith 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 entinostat, 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 entinostat, 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 entinostat, 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 entinostat 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, contract 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 this Offering and Ownership of Our Common Stock

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. You will not have the opportunity, as part of your investment decision, to assess whether we are using the proceeds appropriately. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

We do not know whether an active, liquid and orderly trading market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.

Prior to this offering, no market for shares of our common stock existed and an active trading market for our shares may never develop or be sustained following this offering. Our common stock has been approved for listing on the NASDAQ Global Select Market, however, there is no assurance that it will be listed or, if it is so listed that an active trading market will develop on such exchange. We and the underwriters will determine the initial public offering price based on a number of factors, and such price may not be ultimately indicative of the market price of our common stock after this offering. The market value of our common stock may decrease from the initial public offering price. As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. The lack of an active market may also reduce the fair market value of your shares. Furthermore, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

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 following this offering is likely to be 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 prospectus, 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 entinostat 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 entinostat 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 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 will be influenced by the research and reports that industry or securities analysts publish about us or our business. We do not currently have and may never obtain research coverage by securities and industry analysts. 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.

Prior to this offering, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 78.3% of our outstanding voting stock and, upon completion of this offering, that same group will hold approximately 67.7% of our outstanding voting stock, assuming no exercise of outstanding options. After this offering, this group of stockholders will have the ability to control us through this ownership position even if they do not purchase any additional shares in this offering. 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 Jumpstart Our Business Startups Act of 2012, or 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 this offering; (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 will be 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 will need 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, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be 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. After this offering, we will have outstanding 17,372,675 shares of common stock (including 14,684 shares of unvested restricted stock subject to repurchase by us) based on the number of shares outstanding as of December 31, 2015, assuming: (i) no exercise of the underwriters' over-allotment option; and (ii) the conversion of all outstanding shares of our convertible preferred stock into 12,872,551 shares of common stock immediately prior to the completion of this offering. This includes the shares that we sell in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. Of the remaining shares, 12,972,675 shares of our common stock are currently restricted as a result of securities laws or lock-up agreements but will be able to be sold after this offering as described in the section titled "Shares Eligible for Future Sale" included elsewhere in this prospectus. Moreover, after this offering, holders of an aggregate of 13,259,554 shares of our common stock will 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. We also intend to register all shares of common stock that we may issue under our equity compensation plans. Once we register these shares, they can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described in the section titled "Underwriting" included elsewhere in this prospectus.

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 that will become effective immediately prior to the completion of this offering, 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.

Our amended and restated certificate of incorporation that will become effective upon the closing of this offering will provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for certain litigation that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, employees or agents.

Our amended and restated certificate of incorporation that will become effective upon the closing of this offering will provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for: (i) any derivative action or proceeding brought on behalf of the company; (ii) any action or proceeding commenced by any of our stockholders (including any class action) asserting a claim of breach of a fiduciary duty owed to the company, or other wrongdoing, by any director, officer,

employee or agent of the company or the company's stockholders; (iii) any action or proceeding commenced by any of our stockholders (including any class action) asserting a claim against the company arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws, each of which will become effective upon the closing of this offering; (iv) any action or proceeding commenced by any of our stockholders (including any class action) to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws; or (v) any action or proceeding commenced by any of our stockholders (including any class action) asserting a claim against the company governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit our stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, employees or agents, which may discourage such lawsuits against us and our directors, officers, employees and agents. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business, financial condition or results of operations.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

Some of the statements made in the sections titled "Prospectus Summary," "Risk Factors," "Use of Proceeds," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Business" and elsewhere in this prospectus constitute forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "would," "plan," "anticipate," "believe," "estimate," "predict," "potential," "intend" or "continue," or the negative of these terms or other comparable terminology.

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 commencement, progress and receipt of data from the planned Phase 1b/2 clinical trials of entinostat in lung cancer, melanoma, ovarian cancer and triple negative breast cancer;
- the timing of the commencement, progress and receipt of data from the planned Phase 3 clinical trial of entinostat in advanced HR+ breast cancer;
- the 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 from a completed clinical trial in a future clinical trial;
- our expectations regarding the potential safety, efficacy or clinical utility of entinostat;
- our ability to obtain and maintain regulatory approval for entinostat and the timing or likelihood of regulatory filings and approvals for entinostat;
- our ability to maintain our license with Bayer and KHK;
- the implementation of our strategic plans for our business and entinostat development;
- the scope of protection we establish and maintain for intellectual property rights covering entinostat and our technology;
- the market adoption of entinostat by physicians and patients; and
- developments relating to our competitors and our industry.

These statements are only current predictions and are subject to known and unknown risks, uncertainties and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements. We discuss many of these risks in this prospectus in greater detail in the section titled "Risk Factors" and elsewhere in this prospectus. You should not rely upon 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, after the date of this prospectus, we are under no duty to update or revise any of the forward-looking statements, whether as a result of new information, future events or otherwise.

This prospectus also contains estimates, projections and other information concerning our industry, the market and our business. 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. We obtained the industry, market and competitive position data in this prospectus from our own internal estimates and research as well as from industry and general publications and research surveys and studies conducted by third parties.

USE OF PROCEEDS

We estimate that our net proceeds from the sale of shares of our common stock in this offering will be approximately $46.3 million, based on an initial public offering price of $12.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that our net proceeds will be approximately $53.7 million based on an initial public offering price of $12.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations, establish a public market for our common stock and to facilitate our future access to the public capital markets. We currently expect to use the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, for the following purposes:

- approximately $28.0 million to support the clinical trials of entinostat in combination with *Keytruda*® (pembrolizumab), atezolizumab and avelumab through the expected completion date of the two Phase 2 clinical trials;
- approximately $10.0 million to support additional clinical trials of entinostat in combination with immune checkpoint inhibitors;
- approximately $19.0 million to support the Phase 3 clinical trial of entinostat in advanced HR+ breast cancer through the primary endpoint of overall survival data;
- approximately $16.0 million to conduct activities to support the filing of a New Drug Application for entinostat, including manufacturing of registration batches of active pharmaceutical ingredient and final drug product; and
- the remainder for working capital and general corporate purposes.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures depend on numerous factors, including the ongoing status of and results from our clinical trials and other studies and any unforeseen cash needs. As a result, our management will have broad discretion in applying the net proceeds from this offering. We may use a portion of the net proceeds from this offering allocated to general corporate purposes for the acquisition or licensing, as the case may be, of product candidates, technologies, compounds, other assets or complementary businesses; however, we have no current understandings, agreements or commitments to do so. Pending these uses, we intend to invest the net proceeds from this offering in interest-bearing, investment-grade securities.

Although it is difficult to predict future liquidity requirements, we believe that the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, will fund our projected operating expenses and capital expenditure requirements for at least the next 24 months.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business and do not intend to declare or pay any cash dividends in the foreseeable future. As a result, you will likely need to sell your shares of common stock to realize a return on your investment, and you may not be able to sell your shares at or above the price you paid for them. Payment of cash dividends, if any, in the future will be at the discretion of our board of directors and will depend on then-existing conditions, including our financial condition, operating results, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments and our capitalization as of December 31, 2015, on:

- an actual basis;
- a pro forma basis giving effect to the conversion of all outstanding shares of our convertible preferred stock outstanding as of December 31, 2015 into an aggregate of 12,872,551 shares of our common stock upon completion of this offering and the reclassification of the common stock warrant liability to additional paid-in capital; and
- a pro forma as adjusted basis giving additional effect to the sale of 4,400,000 shares of common stock in this offering at an initial public offering price of $12.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, as if the sale of the shares in this offering had occurred on December 31, 2015.

The information in this table is illustrative only and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this table in conjunction with the information contained in the sections titled “Use of Proceeds,” “Selected Consolidated Financial Data” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” as well as the consolidated financial statements and related notes thereto included elsewhere in this prospectus.

	December 31, 2015		
(in thousands, except share and per share amounts)	Actual	Pro Forma	Pro Forma as Adjusted
		(unaudited)	
Cash, cash equivalents and short-term investments	$ 86,489	$ 86,489	$ 134,039
Convertible preferred stock, par value $0.001: 16,598,980 shares authorized, 12,732,466 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	$ 319,113	—	—
Stockholders’ (deficit) equity:			
Series A convertible preferred stock, par value $0.001: 3,512,194 shares authorized, 700,435 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	7,231	—	—
Common stock, par value $0.0001: 20,800,000 shares authorized, 85,440 shares issued and outstanding, actual[1]; 100,000,000 shares authorized, 12,957,991 shares issued and outstanding, pro forma[1]; 100,000,000 shares authorized, 17,357,991 shares issued and outstanding, pro forma as adjusted[1]	1	2	2
Preferred stock, par value $0.001: no shares authorized, issued and outstanding, actual; 10,000,000 shares authorized, no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	—
Additional paid-in capital	—	329,191	375,495
Accumulated other comprehensive income	28	28	28
Accumulated deficit	(259,675)	(259,675)	(259,675)
Total stockholders’ (deficit) equity	(252,415)	69,546	115,850
Total capitalization	$ 66,698	$ 69,546	$ 115,850

(1) Excludes 14,684 shares of unvested restricted stock subject to repurchase by us.

The number of shares of our common stock outstanding immediately following this offering set forth above is based on 17,357,991 shares of our common stock outstanding as of December 31, 2015, which gives effect to the pro forma transactions described above and excludes the following:

- 2,606,195 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2015 under the 2007 Plan at a weighted-average exercise price of $7.56 per share;
- 355,857 shares of our common stock issuable upon the exercise of the Bayer Warrant at an exercise price of $1.54 per share, based upon 19,978,870 shares of our common stock outstanding as of December 31, 2015 on a fully diluted basis immediately following this offering, which warrant is expected to remain outstanding upon completion of this offering;
- 14,684 shares of unvested restricted stock subject to repurchase by us;
- 1,750,000 shares of our common stock reserved for issuance under the 2015 Plan, which will become effective upon completion of this offering, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2015 Plan; and
- 250,000 shares of our common stock reserved for issuance under the ESPP, which will become effective upon completion of this offering, as well as any future increases in the number of shares of our common stock reserved for issuance under the ESPP.

DILUTION

If you invest in our common stock in this offering, your ownership interest will be immediately diluted to the extent of the difference between the assumed initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering. Net tangible book value per share of our common stock is determined at any date by subtracting our total liabilities and convertible preferred stock from the amount of our total tangible assets (total assets less intangible assets) and dividing the difference by the number of shares of our common stock deemed to be outstanding at that date.

Our historical net tangible book deficit as of December 31, 2015 was $(252.4) million, or $(2,954.30) per share, based on 85,440 shares of common stock outstanding as of December 31, 2015 (excluding 14,684 shares of unvested restricted stock subject to repurchase by us). Our pro forma net tangible book value as of December 31, 2015 was approximately $69.5 million, or $5.37 per share. Our pro forma net tangible book value per share gives effect to the conversion of all outstanding shares of our convertible preferred stock outstanding as of December 31, 2015 into an aggregate of 12,872,551 shares of our common stock upon completion of this offering.

After giving effect to our receipt of approximately $46.3 million of estimated net proceeds, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, from our sale of common stock in this offering at an initial public offering price of $12.00 per share, our pro forma as adjusted net tangible book value as of December 31, 2015, would have been $115.9 million, or $6.67 per share. This amount represents an immediate increase in net tangible book value of $1.30 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of $5.33 per share of our common stock to new investors purchasing shares of common stock in this offering.

The following table illustrates this dilution on a per share basis to new investors:

Assumed initial public offering price per share		$12.00
Historical net tangible book deficit per share as of December 31, 2015	$(2,954.30)	
Pro forma increase in net tangible book value per share attributable to pro forma transactions and other adjustments described above	2,959.67	
Pro forma net tangible book value per share before this offering	5.37	
Pro forma increase in net tangible book value per share attributable to new investors	1.30	
Pro forma as adjusted net tangible book value per share after this offering		6.67
Dilution per share to new investors purchasing common stock in this offering		$ 5.33

If the underwriters exercise their over-allotment option in full, the pro forma as adjusted net tangible book value per share after giving effect to this offering would be $6.84 per share, which amount represents an immediate increase in pro forma net tangible book value of $1.47 per share of our common stock to existing stockholders and an immediate dilution in net tangible book value of $5.16 per share of our common stock to new investors purchasing shares of common stock in this offering.

The following table summarizes, as of December 31, 2015, after giving effect to the pro forma adjustments noted above, the differences between the number of shares purchased from us, the total consideration paid to us, and the average price per share paid to us by existing stockholders and by new

investors purchasing shares in this offering, before deducting underwriting discounts and commissions and estimated offering expenses payable by us, at an initial public offering price of $12.00 per share.

(in thousands, except per share amounts)	Shares Purchased		Total Cash Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders	12,958	75%	$188,089	78%	$ 14.52
New investors	4,400	25%	52,800	22%	12.00
Total	17,358	100%	$240,889	100%	$ 13.88

The number of shares of our common stock outstanding immediately following this offering is based on 17,357,991 shares of our common stock outstanding as of December 31, 2015, which gives effect to the pro forma transactions described above and excludes the following:

- 2,606,195 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2015 under the 2007 Plan at a weighted-average exercise price of $7.56 per share;
- 355,857 shares of our common stock based upon 19,978,870 shares of our common stock outstanding as of December 31, 2015 on a fully diluted basis immediately following this offering, issuable upon the exercise of the Bayer Warrant at an exercise price of $1.54 per share, which warrant is expected to remain outstanding upon completion of this offering;
- 14,684 shares of unvested restricted stock subject to repurchase by us;
- 1,750,000 shares of our common stock reserved for issuance under the 2015 Plan, which will become effective upon completion of this offering, as well as any future increases in the number of shares of our common stock reserved for issuance under the 2015 Plan; and
- 250,000 shares of our common stock reserved for issuance under the ESPP, which will become effective upon completion of this offering, as well as any future increases in the number of shares of our common stock reserved for issuance under the ESPP.

If all our outstanding stock options had been exercised as of December 31, 2015, assuming the treasury stock method, our pro forma net tangible book value as of December 31, 2015 (calculated on the basis of the assumptions set forth above) would have been approximately $72.1 million, or $5.47 per share of our common stock, and the pro forma as adjusted net tangible book value would have been $6.74 per share, representing dilution in our pro forma as adjusted net tangible book value to new investors of $5.26 per share.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital by issuing equity securities or convertible debt, your ownership will be further diluted.

Effective upon completion of this offering, 1,750,000 shares of our common stock will be reserved for future issuance under our 2015 Plan and 250,000 shares of our common stock will be reserved for future issuance under our ESPP, and the number of reserved shares under each such plan will also be subject to automatic annual increases in accordance with the terms of the plans. New awards that we may grant under our 2015 Plan or shares issued under our ESPP will further dilute investors purchasing common stock in this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected consolidated financial data together with the information contained in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes, included elsewhere in this prospectus. We have derived the consolidated statements of operations data for the years ended December 31, 2014 and 2015 and the consolidated balance sheet data as of December 31, 2014 and 2015 from our audited consolidated financial statements, included elsewhere in this prospectus. Our historical results are not necessarily indicative of results to be expected for the full year or any period in the future.

(in thousands, except share and per share data)	Years Ended December 31, 2014	2015
Consolidated Statements of Operations Data:		
Revenues:		
License fees	$ —	$ 627
Total revenues	—	627
Operating expenses:		
Research and development	10,175	9,549
General and administrative	11,157	11,591
Total operating expenses	21,332	21,140
Loss from operations	(21,332)	(20,513)
Other income (expense):		
Interest income	10	161
Interest expense	(299)	(1,575)
Change in fair value of common stock warrant liability	1,789	(2,155)
Other income (expense), net	4	(37)
Total other income (expense)	1,504	(3,606)
Net loss	$(19,828)	$ (24,119)
Net loss attributable to common stockholders—basic and diluted[1]	$(26,357)	$ (103,845)
Net loss per share attributable to common stockholders—basic and diluted[1]	$(453.02)	$ (1,519.27)
Weighted-average common shares outstanding used to compute net loss per share attributable to common stockholders—basic and diluted[1]	58,181	68,352
Pro forma net loss per share attributable to common stockholders—basic and diluted[1]		$ (2.28)
Pro forma weighted-average common shares outstanding used to compute net loss per share attributable to common stockholders, basic and diluted[1]		9,597,519

(1) See Note 2 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the weighted-average number of shares used in the computation of the per share amounts.

(in thousands)	As of December 31, 2014	As of December 31, 2015
Consolidated Balance Sheet Data:		
Cash, cash equivalents and short-term investments	$ 12,091	$ 86,489
Total assets	12,816	89,903
Current portion of long-term debt	1,449	—
Convertible notes	5,000	—
Long-term debt, less current portion	7,435	—
Common stock warrant liability	693	2,848
Convertible preferred stock	146,853	319,113
Accumulated deficit	(159,801)	(259,675)
Total stockholders' deficit	(152,569)	(252,415)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section titled, "Selected Consolidated Financial Data," and our consolidated financial statements and related notes thereto included elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the section titled "Risk Factors," our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a clinical stage biopharmaceutical company developing entinostat as a combination therapy in multiple cancer indications with our initial focus on tumors that have shown sensitivity to immunotherapy, including lung cancer, melanoma, ovarian cancer and triple negative breast cancer, or TNBC. Entinostat is our oral, small molecule drug 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 900 cancer patients. We are currently evaluating entinostat in combination with *Keytruda*® (pembrolizumab) in a Phase 1b/2 clinical trial, ENCORE 601, for non-small cell lung cancer, or NSCLC, and melanoma, and we plan to initiate a Phase 1b/2 clinical trial, ENCORE 602, for entinostat in combination with atezolizumab in TNBC in the first half of 2016 and a Phase 1b/2 clinical trial, ENCORE 603, for entinostat in combination with avelumab in ovarian cancer in the second half of 2016. We have also entered into a collaboration with Ares Trading S.A., a subsidiary of Merck KGaA, Darmstadt, Germany, or Merck KGaA, and Pfizer, Inc., to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with an investigational monoclonal antibody targeting PDL-1, avelumab, in a Phase 1b/2 clinical trial, ENCORE 603, of patients with ovarian cancer. 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.

We are also developing entinostat for use in advanced hormone receptor positive, or HR+, breast cancer. Following positive results from our Phase 2b clinical trial, ENCORE 301, entinostat in combination with *Aromasin*® (exemestane tablets) was granted breakthrough therapy designation by the U.S. Food and Drug Administration, or the FDA, in advanced HR+ breast cancer for which it is currently being evaluated in a Phase 3 clinical trial.

We have no products approved for commercial sale and have not generated any product revenues from product sales to date, and 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, 2014 and 2015, we reported a net loss of $19.8 million and $24.1 million, respectively. As of December 31, 2015, we had an accumulated deficit of $259.7 million, which included non-cash charges for stock-based compensation, preferred stock accretion and extinguishment charges. As of December 31, 2015, we had cash, cash equivalents and short-term investments of $86.5 million.

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 candidate, entinostat.

Our revenues in 2015 have been derived from our license agreement with Kyowa Hakko Kirin Co., Ltd., or KHK, under which we granted KHK an exclusive license to develop and commercialize entinostat in Japan and Korea, or the KHK license agreement. In 2015, we received a $25.0 million upfront payment from KHK, inclusive of an equity investment, and to the extent certain development and commercial milestones are achieved, we will receive up to $75.0 million in milestone payments from KHK over the term of the KHK license agreement. Under the terms of the KHK license agreement, we are responsible for the manufacture and supply of the product during the development activities and we are obligated to provide KHK with access to know-how and regulatory information that we may develop over the life of the entinostat patent. We allocated $17.3 million of the upfront payment to the upfront license fee and determined that there are two units of accounting in connection with our obligations at inception under the KHK license agreement: (i) license unit of accounting and (ii) rights to additional intellectual property. The two deliverables identified above comprise the license unit of accounting. We 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 license fee will be allocated to the license unit of accounting. The arrangement consideration allocated to the license unit of accounting will be recognized as revenue ratably over our expected services period (currently expected to be through 2029) commencing on the date of the first delivery of the clinical trial materials, which occurred during the second quarter of 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.

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 entinostat, which include:

- expenses incurred under agreements related to our clinical trials, including the costs for investigative sites and contract research organizations, or CROs, that conduct our clinical trials;
- employee-related expenses related to our research and development activities, including salaries, benefits, travel and 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. 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.

As we expand the clinical development of entinostat, 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. We have incurred a total of $71.8 million in research and development expenses from our inception through December 31, 2015.

Conducting a significant amount of research and development is 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 seek to complete the development of entinostat. The successful development of entinostat 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 entinostat for the period, if any, in which material net cash inflows from these potential drug 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 salaries and related benefits, including stock-based compensation, related to our executive, finance, business development and support functions. Other general and administrative expenses include facility-related costs not otherwise allocated to research and development expenses, travel expenses for our general and administrative personnel and professional fees for auditing, tax, and legal services. We anticipate that our general and administrative expenses will increase in future periods, reflecting both increased costs in connection with the potential future commercialization of entinostat, an expanding infrastructure and increased professional fees associated with being a public reporting company.

Sales and Marketing

Selling and marketing expenses consist primarily of salaries and benefits for employees in the marketing, commercial and sales functions. Other significant expenses include professional and consulting fees related to these functions. Though we have incurred immaterial sales and marketing expenses to date as we continue primarily with the clinical development of our drug candidate programs, we expect to begin to incur increased selling and marketing expenses in anticipation of the commercialization of entinostat. These increased expenses will include payroll-related costs as we add employees in the commercial departments, costs related to the initiation and operation of our sales and distribution network and marketing related costs.

Interest Income (Expense), Net

Interest income consists of interest income earned on our cash, cash equivalents and short-term investment balances. Interest expense consists 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 common stock warrant liability is associated with warrants to purchase common stock issued with license agreements. The change in fair value consists 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 are recognized in other income (expense) in the consolidated statements of comprehensive loss.

Change in Fair Value of Derivatives

In 2014, we entered into a loan and security agreement consisting of a term loan facility that included a contingent liability that we determined to be a free-standing derivative. Although the term loans were paid in full during the fourth quarter of 2015, the contingent liability survived and is due and payable upon certain change of control or liquidity events. At each balance sheet date prior to the settlement of the contingent liability, we calculate the fair value of this right using a probability-weighted expected-return model, or PWERM. Gains and losses arising from changes in fair value are recognized in other income (expense) in the consolidated statements of comprehensive loss.

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 1 to our audited consolidated financial statements included elsewhere in this prospectus, 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 is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses during the reporting periods. These items are monitored and analyzed by us for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances; the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates.

While our significant accounting policies are more fully described in Note 1 to our consolidated financial statements included elsewhere in this prospectus, 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. The majority of our service providers invoice us monthly in arrears for services performed. 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 statements of comprehensive loss based

on their fair values. 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 stock-based awards on a straight-line basis over the vesting period of the award for employees and non-employees, which is generally four years. Compensation expense related to our stock-based awards is subject to a number of estimates, including the estimated volatility and underlying fair value of our common stock as well as the estimated life of the awards. For a detailed description of how we estimate fair value for purposes of option grants and the methodology used in measuring stock-based compensation expense, see "Stock-Based Compensation and Common Stock Valuations" below. Following the completion of this offering, stock option values will be determined based on the market price of our common stock on the NASDAQ Global Select Market.

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 statements of comprehensive loss 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 initial public offering, or IPO, or other change of control events. The estimated fair value was determined using a PWERM approach. The fair value of the derivative will be re-measured at each balance sheet date until the liability is settled and any changes in the fair value of the derivative liability will be recorded in other income (expense) in the consolidated statements of comprehensive loss.

Stock-Based Compensation and Common Stock Valuations

Stock-Based Compensation

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including (a) the expected volatility of our stock, (b) the expected term of the award, (c) the risk-free interest rate (d) expected dividends and (e) the fair value of our common stock on the date of grant. Due to the lack of a public market for the trading of our common stock and a lack of company-specific historical and implied volatility data, we have based our estimates of expected volatility on the historical volatility of a group of publicly traded companies in the life sciences and biotechnology industries generally in a similar stage of development as ourselves. For these analyses, we have selected companies that we consider broadly comparable to our company and with historical share price information sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this methodology until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. For options granted to employees in 2014 and 2015, we determined the

expected term based on an average of expected terms used by a peer group of similar public companies. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted.

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.

We have computed the fair value of employee and non-employee stock options at date of grant using the following weighted-average assumptions:

	Years Ended December 31,	
	2014	2015
Expected term (in years)	5.96	5.89
Volatility rate	70.36%	69.92%
Risk-free interest rate	1.91%	1.73%
Expected dividend yield	0.00%	0.00%

Stock-based compensation for employees and non-employees was allocated as outlined below (in thousands):

	Years Ended December 31,	
(in thousands)	2014	2015
Research and development	$ 527	$ 846
General and administrative	1,730	3,036
Total	$ 2,257	$ 3,882

As of December 31, 2015, total unrecognized compensation expense was $9.1 million, net of related forfeiture estimates; and the weighted-average remaining requisite service period was 3.2 years. We expect the impact of our stock-based compensation expense for stock options granted to employees and non-employees to grow in future periods due to the potential increases in the value of our common stock and in headcount.

Common Stock Valuations

We are a private company with no public market for our common stock. Therefore, our board of directors determines the fair value of our common stock considering, in part, the work of an independent third-party valuation specialist. The valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the Practice Aid. In conducting these valuations, our board of directors considered all objective and subjective factors that it believed to be relevant, including its and management's best estimates of our business condition, prospects and operating performance at each grant date. The valuations, assumptions and methodologies included, among other things:

- any recent contemporaneous third-party valuations prepared in accordance with methodologies outlined in the Practice Aid;

- the prices of our convertible preferred stock sold to investors in arm's length transactions and the rights, preferences and privileges of our convertible preferred stock as compared to those of our common stock, including the liquidation preferences of our convertible preferred stock;
- our results of operations, financial position and the status of research and development efforts;
- the lack of liquidity of our common stock as a private company;
- our stage of development and business strategy and the material risks related to our business and industry;
- the composition of, and changes to, our management team and board of directors;
- the achievement of enterprise milestones, including entering into collaboration and license agreements;
- the valuation of comparable publicly traded companies in the life science and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- the likelihood of achieving a liquidity event for our stockholders, such as an IPO or a sale of our company, given prevailing market conditions; and
- any external market conditions affecting the life science and biotechnology sectors.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event and the determinations of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per common share could have been significantly different. The valuations are highly complex and subjective.

Common Stock Valuation Methodologies

In valuing our common stock, we used the market approach, which is based on the assumption that the value of an asset is equal to the value of a substitute asset with the same characteristics. The following market approaches were utilized in our valuations:

- **Guideline Public Company Method**. The guideline public company market approach estimates the value of a business by comparing a company to comparable publicly traded companies.
- **Precedent Transaction Method**. The precedent transaction market approach estimates the value of a business based on the utilization of a company's own relevant stock transactions.

In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. We selected the PWERM approach to allocate the equity value among the various share classes given our stage of development, the availability of relevant data and our expectation that we are able to forecast distinct future liquidity scenarios as of each valuation date. Under the PWERM approach, share value is derived from the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class. For each valuation, the fair value of our

common stock was estimated using a probability-weighted analysis of the present value of the returns afforded to our common stockholders under several future exit or liquidity event scenarios, including (1) an IPO, (2) a trade sale of our company at a high premium to the cumulative amounts invested by our convertible preferred stock investors, or trade sale high, (3) a trade sale of our company at a lesser premium to the cumulative amounts invested by convertible preferred stock investors, or trade sale low and (4) a trade sale of our company at a value below the cumulative amounts invested by convertible preferred stock investors, or trade sale below liquidation preference.

After the projected equity value in each scenario was allocated to the various share classes, we calculated the present value of each share class using an appropriate risk-adjusted discount rate based on consideration of the venture capital rates of return detailed in the Practice Aid and an analysis of other quantitative and qualitative factors considered pertinent to estimating the discount rate. Next, we applied a discount for lack of marketability to our common shares because we were valuing a minority interest in our company as a closely held, non-public company with no liquid market for its shares. The discount for lack of marketability was based on quantitative models (protective put option calculation), as well as empirical studies of restricted stock issued by publicly traded companies and private placements by pre-IPO companies. We also considered the rights and privileges of our convertible preferred stock relative to our common stock, including anti-dilution protection, cumulative dividend rights, protective provisions in our certificate of incorporation and rights to participate in future rounds of financing. Finally, we assigned a probability weighting to each scenario based on our estimate of the likelihood of occurrence, as of each valuation date. In each case the future projected enterprise values were based on a review of both guideline IPO and M&A transactions involving life science and biotechnology companies that we considered broadly comparable to our company.

For valuations after the completion of this offering, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock on the date of grant, as reported on the NASDAQ Global Select Market.

Stock Option Grants

The following table summarizes stock options granted from January 1, 2014 through February 26, 2016:

	Number of Common Shares Underlying Options Granted	Exercise Price Per Common Share	Fair Value Per Common Share	Intrinsic Value Per Common Share at Grant Date
January 23, 2014	86,277[1]	$ 21.07	$ 21.07	$ —
February 4, 2014	86,608[1]	$ 21.07	$ 21.07	$ —
February 25, 2014	11,393	$0.00154	$ 21.07	$ 21.06
September 4, 2014	390	$ 6.32	$ 6.32	$ —
September 15, 2014	265,475[2]	$ 6.32	$ 6.32	$ —
December 18, 2014	103,071	$ 6.35	$ 6.35	$ —
June 1, 2015	446,852	$ 7.20	$ 7.20	$ —
June 1, 2015	11,393[3]	$0.00154	$ 7.20	$ 7.19
June 30, 2015	548,223	$ 7.20	$ 7.20	$ —
August 18, 2015	246,479	$ 7.20	$ 10.90	$ 3.70
August 20, 2015	24,000	$ 7.20	$ 10.90	$ 3.70
September 9, 2015	636,947	$ 10.90	$ 10.90	$ —
December 2, 2015	20,240	$ 11.13	$ 11.13	$ —
January 15, 2016	137,600	$ 11.13	$ 11.13	$ —
February 17, 2016	12,880	$ 11.13	$ 11.13	$ —

(1) On September 15, 2014, 265,475 options with exercise prices ranging from $15.38 to $47.67, including all of the options issued on January 23, 2014 and February 4, 2014, were canceled in connection with an option exchange program with existing option holders for an aggregate 265,475 options priced at $6.32.
(2) These options were granted in connection with an option exchange program with existing option holders.
(3) This option was granted as a replacement option for the option granted on February 25, 2014, which expired on December 31, 2014.

The intrinsic value of all outstanding options as of December 31, 2015 was $11.7 million based on the estimated fair value of our common stock of $12.00 per share, of which approximately $4.8 million related to vested options and approximately $6.9 million related to unvested options.

Results of Operations

Comparison of the Years Ended December 31, 2014 and 2015:

(in thousands)	Years Ended December 31, 2014	2015	Increase (Decrease) $	%
Revenues:				
License fees	$ —	$ 627	$ 627	100%
Total revenues	—	627	627	100%
Operating expenses:				
Research and development	10,175	9,549	(626)	(6)%
General and administrative	11,157	11,591	434	4%
Total operating expenses	21,332	21,140	(192)	(1)%
Loss from operations	(21,332)	(20,513)	(819)	(4)%
Other income (expense):				
Interest income	10	161	151	NM
Interest expense	(299)	(1,575)	1,276	NM
Change in fair value of common stock warrant liability	1,789	(2,155)	3,944	NM
Other income (expense), net	4	(37)	41	NM
Total other income (expense)	1,504	(3,606)	5,110	NM
Net loss	$(19,828)	$(24,119)	$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, 2014	2015	Increase (Decrease) $	%
External research and development expenses	$ 7,241	$ 5,957	$(1,284)	(18)%
Internal research and development expenses	2,934	3,592	658	22%
Total research and development expenses	$10,175	$ 9,549	$ (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 Income

For the year ended December 31, 2015, interest income increased $0.2 million from the prior year. The increase was due to interest earned on our cash, cash equivalents and short-term investments from the $25.0 million of proceeds from the licensing fees and equity investment under the KHK license and stock purchase agreements, which were received during the first quarter of 2015, the $18.7 million of gross proceeds from the Series C-1 financing, which were received during the second quarter of 2015 and the $61.3 million of gross proceeds from the Series C-1 financing, which were received during the third quarter of 2015.

Interest Expense

For the year ended December 31, 2015, interest expense increased $1.3 million to $1.6 million from $0.3 million in the prior year. The increase was due to interest expense on the $5.0 million convertible notes that were issued during the third quarter of 2014 as well as interest expense on the $9.0 million in term loans that were funded in September and December of 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 statements of comprehensive loss. Upon the completion of our IPO, the warrant will be reclassified to additional paid-in capital.

Liquidity and Capital Resources

Since our inception and through December 31, 2015, we have raised an aggregate of $185.8 million to fund our operations from the sale of convertible preferred stock and convertible debt securities. As of December 31, 2015, our cash, cash equivalents and short-term investments were $86.5 million.

We have incurred losses and cumulative negative cash flows from operations since our inception; and as of December 31, 2015, we had an accumulated deficit of $259.7 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.

In June 2015, we issued 1,712,559 shares of our Series C-1 convertible preferred stock for $18.5 million in cash, net of offering costs of $0.2 million, and the conversion of the outstanding principal on the convertible notes of $5.0 million that were issued during the third quarter of 2014 and related accrued interest of $0.2 million. In August 2015, we issued an additional 4,377,902 shares of our Series C-1 convertible preferred stock for $61.1 million, net of offering costs of $0.2 million.

As further discussed below in the section titled “Indebtedness,” we prepaid the $8.3 million outstanding balance of the loan and security agreement with Solar Capital Ltd., or Solar, plus accrued interest and a final fee and prepayment penalty on during the fourth quarter of 2015.

Indebtedness

Solar Capital Ltd.

In June 2014, we entered into a loan and security agreement with 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 our existing and after-acquired assets except our 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. Our intellectual property is subject to a negative pledge. In September and December 2014, we amended the term loan facility. The term loan facility had a maturity date in June 2018.

In September 2014, the initial term loan was funded in the aggregate principal amount of $5.0 million. In December 2014, an additional term loan in the aggregate principal amount of $4.0 million was funded with the post-closing condition that we enter into a strategic transaction in Japan or Korea and receive $7.5 million in net equity proceeds and $17.5 million in license-related proceeds. We received the $7.5 million in net equity proceeds in full in January 2015, pursuant to the Series B-1 preferred stock purchase agreement with KHK, or the KHK stock purchase agreement, and $17.5 million in license-related proceeds in full in February 2015, pursuant to the KHK license agreement.

During the fourth quarter of 2015, we prepaid the outstanding balance of 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. We recorded an

expense of $0.3 million for the final fee and prepayment penalty we were required to pay and wrote off $0.3 million of unamortized debt discount and deferred issuance costs related to the term loans. As of December 31, 2015, no amount was outstanding under this term loan facility.

Interest accrued on the term loans at a floating rate per annum equal to LIBOR plus 8.8%, payable monthly in arrears. In connection with the term loan facility, we paid a closing fee of $170,000 and other transactional and legal costs of $140,000. Upon the completion of this offering, we will be required to pay a $150,000 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. In connection with the prepayment of the term loans, we were required to pay, and paid, 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. We were required to make interest-only payments on the funded term loans until July 1, 2015. Beginning on July 1, 2015, we were required to make consecutive monthly payments of principal plus accrued interest in equal monthly installments until the maturity date. We had the option to prepay the term loans provided we pay a prepayment fee equal to 2% of the outstanding principal if paid prior to the one-year anniversary of the funding and 1% of the outstanding principal if paid after the one-year anniversary of the funding. We paid 1% of the outstanding principal as a prepayment penalty during the fourth quarter of 2015.

2014 Convertible Notes

In September 2014, we entered into a bridge loan financing with various investors, in which we issued for an aggregate principal amount of $5.0 million (the 2014 Notes). We received $4.9 million in the first closing, which occurred in September 2014, and received $0.1 million in the second closing, which occurred in October 2014. The 2014 Notes accrued interest at 6% per annum and had a maturity date of September 30, 2015 and were convertible upon the occurrence of certain events during the period that the 2014 Notes were outstanding. In June 2015, as a result of the first close of our Series C-1 financing, the 2014 Notes and the related interest of $0.2 million were converted into 372,446 shares of our Series C-1 convertible preferred stock at an original issuance price of $14.00 per share, which was the price paid by other investors in the financing.

Plan of Operations and 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 believe that the net proceeds from this offering, together with our existing cash and cash equivalents, will fund our projected operating expenses and capital expenditure requirements through the end of 2017.

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 drug candidate 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 for entinostat;
- 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 entinostat;
- 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 entinostat if entinostat 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 become a public company.

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 payments under our agreements with them, we will not have any committed external source of liquidity.

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:

	Years Ended December 31,	
(in thousands)	**2014**	**2015**
Net cash used in operating activities	$(14,393)	$ (2,428)
Net cash provided by (used in) investing activities	1,888	(61,669)
Net cash provided by financing activities	12,410	77,267
Net (decrease) increase in cash and cash equivalents	$ (95)	13,170

Net Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2014 was $14.4 million compared to $2.4 million of net cash used in operating activities for the year ended December 31, 2015. The decrease in cash used in operating activities for the year ended December 31, 2015 of $12.0 million was primarily due to increases in deferred revenue of $16.7 million and in accounts payable of $1.8 million partially offset by an increase in our net loss of $2.0 million (adjusted for non-cash items) and by increases in deposits of $0.8 million and prepaid and other assets of $0.5 million and a decrease in accrued expenses and other liabilities of $3.2 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. Our net loss for the year ended December 31, 2014, adjusted for non-cash items such as stock-based compensation, change in fair value of derivative, change in fair value of warrants and amortization and accretion, was $15.0 million, compared to $17.0 million for the year ended December 31, 2015.

Net Cash Provided by Investing Activities

Net cash provided by investing activities for the year ended December 31, 2014 was $1.9 million compared to net cash used in investing activities of $61.7 million for the year ended December 31, 2015. The increase in cash used in investing activities of $63.6 million was primarily due to the purchases of short-term investments, net of sales and maturities, from the $25.0 million of proceeds from the licensing fees and equity investment under the KHK license and stock purchase agreements, which were received during the first quarter of 2015, the $18.7 million of gross proceeds from the Series C-1 financing, which were received during the second quarter of 2015 and the $61.3 million of gross proceeds from the Series C-1 financing, which were received during the third quarter of 2015.

Net Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2014 was $12.4 million compared to $77.3 million for the year ended December 31, 2015. During the year ended December 31, 2014, we received $9.0 million proceeds from the term loans and $5.0 million from the issuance of convertible debt in the form of convertible notes, which was partially offset by $1.6 million of deferred issuance costs related to preparing for an IPO in 2014 and debt issuances. During the year ended December 31, 2015, we received the proceeds from the KHK license and stock purchase agreements, of which $7.7 million related to the issuance of the Series B-1, and proceeds from the Series C-1 financings of $79.6 million, net of $0.4 million of issuance costs, which was partially offset by the $9.0 million early repayment of the term loans during the fourth quarter of 2015.

Contractual Obligations and Contingent Liabilities as of December 31, 2015

The following table summarizes our significant contractual obligations as of December 31, 2015:

(in thousands)	Total	Less than 1 Year	1 to 3 Years	3 to 5 Years	More than 5 Years
Operating leases for office space[1]	$1,328	$ 304	$498	$484	$ 42
Capital lease for office equipment[2]	10	3	4	3	—
	$1,338	$ 307	$502	$487	$ 42

(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. On December 22, 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 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.

(2) In December 2013, we entered into a 60-month 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 agreements we have entered into with various entities pursuant to which we have in-licensed certain intellectual property, including the Bayer license agreement. See "Business—Intellectual Property—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.

In March 2014, we entered into a clinical trial agreement with Eastern Cooperative Oncology Group, a contracting entity for ECOG-ACRIN, that describes the parties' obligations with respect to the NCI-sponsored pivotal Phase 3 clinical trial of entinostat. We 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, we are obligated to supply entinostat and placebo to ECOG-ACRIN for use in the clinical trial. As of the effective date of the amendment to the clinical trial agreement, our aggregate payment obligations under this agreement were approximately $20.6 million. As of December 31, 2015, our remaining payment obligations under this agreement are approximately $18.3 million over an estimated period of approximately seven years.

Merck KGaA-Pfizer Collaboration—On December 31, 2015, we entered into a clinical trial collaboration and supply agreement with Merck KGaA and Pfizer, or the Alliance, under which we will conduct a clinical trial evaluating entinostat in combination with an investigational monoclonal antibody, avelumab, in patients with ovarian cancer. We will share the study costs equally with the Alliance. See Note 3 for further discussion.

Net Operating Loss and Research and Development Tax Credit Carryforwards

At December 31, 2015, we had federal and state tax net operating loss carryforwards of $38.6 million and $27.0 million, respectively. The federal and state net operating loss carryforwards expire beginning in 2015 and ending in 2035. At December 31, 2015, we had available income tax credits of $1.5 million, which are available to reduce future income taxes, if any. These income tax credits begin to expire in 2020.

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.

Internal Control Over Financial Reporting

In accordance with the provisions of the Sarbanes-Oxley Act, neither we nor our independent registered public accounting firm has performed an evaluation of our internal control over financial reporting during any period included in this prospectus. However, we and our independent registered public accounting firm previously identified and disclosed control deficiencies in the design and operation of our internal control over financial reporting that constituted a material weakness in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our financial statements will not be prevented or detected on a timely basis. The material weakness identified resulted from the fact that we did not have sufficient financial reporting and accounting staff with appropriate training in GAAP and SEC rules and regulations.

In response to this material weakness, during 2015 we took numerous steps to remediate the underlying causes of the material weakness, including: i) the hiring of additional personnel with the appropriate financial reporting experience to expand our financial management and reporting infrastructure and further develop and document our accounting policies and financial reporting procedures; ii) the retention of an additional accounting firm to provide technical consulting services with respect to complex accounting issues; and iii) the establishment and implementation of policies and procedures to ensure adherence to accounting policies, rules and regulations and to provide enhanced financial analysis and quality control. Accordingly, as of December 31, 2015, we believe we have remediated the previously identified material weakness.

JOBS Act

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

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, 2015, we had cash equivalents of $23.2 million, consisting of interest-bearing money market funds, debt securities of U.S. government agencies and commercial paper and highly rated corporate bonds, and short-term investments of $63.3 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. Due to the short-term maturities of our cash equivalents, an immediate 100 basis point change in interest rates would not have a material effect on the fair market value of our cash equivalents.

We do not believe that inflation and changing prices had a significant impact on our results of operations for any periods presented herein.

BUSINESS

Overview

We are a clinical stage biopharmaceutical company developing entinostat as a combination therapy in multiple cancer indications with our initial focus on tumors that have shown sensitivity to immunotherapy, including lung cancer, melanoma, ovarian cancer and triple negative breast cancer, or TNBC. Entinostat is our oral, small molecule drug 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 900 cancer patients. We are currently evaluating entinostat in combination with *Keytruda*® (pembrolizumab) in a Phase 1b/2 clinical trial for non-small cell lung cancer, or NSCLC, and melanoma, and we plan to initiate a Phase 1b/2 clinical trial for entinostat in combination with atezolizumab in TNBC in the first half of 2016 and a Phase 1b/2 clinical trial for entinostat in combination with avelumab in ovarian cancer in the second half of 2016. 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.

We are also developing entinostat for use in advanced hormone receptor positive, or HR+, breast cancer. Following positive results from our Phase 2b clinical trial, ENCORE 301, entinostat in combination with *Aromasin*® (exemestane tablets) was granted breakthrough therapy designation by the U.S. Food and Drug Administration, or the FDA, in advanced HR+ breast cancer for which it is currently being evaluated in a Phase 3 clinical trial.

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 PDL-1, 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 PDL-1 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. We believe entinostat's well-characterized safety profile and mechanism of action allows it to be readily combined with, and thereby enhance the activity of, conventional and novel cancer therapies, such as immune checkpoint inhibitors, hormone therapies and chemotherapies.

Entinostat is currently being studied in clinical trials across a broad range of solid tumors, including breast cancer, NSCLC and renal cell carcinoma. We are working in collaboration with Merck & Co. Inc., or Merck, to study the combination of entinostat with Merck's immune checkpoint inhibitor, *Keytruda*, in a Phase 1b/2 clinical trial, ENCORE 601, of up to 178 patients with NSCLC or melanoma. The Phase 1b portion of the clinical trial will evaluate the safety and tolerability of the combination of entinostat and *Keytruda* and the Phase 2 portion of the clinical trial will assess the efficacy of entinostat combined with *Keytruda* in patients with either NSCLC or melanoma. Patient enrollment for the Phase 1b portion of the clinical trial was initiated in August 2015. 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 investigational immune checkpoint inhibitor, atezolizumab, in a Phase 1b/2 clinical trial, ENCORE 602, of patients with TNBC. We have also entered into a collaboration with Ares Trading, S.A., a subsidiary of Merck KGaA, Darmstadt, Germany, or Merck KGaA, and Pfizer Inc., or Pfizer, to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with the investigational monoclonal antibody targeting PDL-1, 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-PDL-1 IgG1 monoclonal antibody (MSB0010718C). Additionally, entinostat is being evaluated in two ongoing and one 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.

We are also providing financial and operational support for an ongoing Phase 3 clinical trial in advanced HR+ breast cancer in combination with *Aromasin*. Eastern Cooperative Oncology Group-American College of Radiology Imaging Network Cancer Research Group, or ECOG-ACRIN, is conducting this clinical trial under sponsorship and funding support from the National Cancer Institute, or NCI. The Phase 3 clinical trial 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 were incorporated under the laws of the State of Delaware in October 2005. Since inception, we have focused our efforts on the research and development and raising capital. Based on our research and development plans and our timing expectations related to the progress of our programs, we believe that the net proceeds from this offering, together with our existing cash, cash equivalents and short-term investments, will fund our projected operating expenses and capital expenditure requirements for at least the next 24 months. Our future capital requirements will depend on many factors, including those discussed in the sections titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Risk Factors," included elsewhere in this prospectus.

Clinical Development Programs of Entinostat

The following table sets forth information pertaining to the clinical trials for entinostat with our initial focus on advancing ENCORE 601, ENCORE 602 and ENCORE 603 in immuno-oncology and E2112, our collaboration with ECOG-ACRIN and the NCI, in advanced HR+ breast cancer.

Immuno-Oncology	Preclinical	Phase 1	Phase 2	Phase 3	Indication	Sponsor	Data Expected
ENCORE 601: Entinostat + *Keytruda*					NSCLC / Melanoma	Syndax[1]	First half of 2016
ENCORE 602: Entinostat + atezolizumab					TNBC	Syndax[2]	Second half of 2016
ENCORE 603: Entinostat + avelumab					Ovarian Cancer	Syndax[2]	First half of 2017
J1353: Epigenetic Priming to Immunotherapy					NSCLC	Johns Hopkins[3]	Second half of 2016
NCI-7870: Entinostat + *Proleukin*					Renal cell carcinoma	NCI[4]	January 2016
NCI-9844: Entinostat + *Opdivo* + *Yervoy*					Solid tumors	NCI[5]	Second half of 2017
Advanced HR+ Breast Cancer	Preclinical	Phase 1	Phase 2	Phase 3	Indication	Sponsor	Data Expected
E2112: Entinostat + *Aromasin*					Advanced HR+, HER2- breast cancer	NCI[6]/Syndax	No sooner than second half of 2017 (PFS) 2019 (OS)
Other Indications	Preclinical	Phase 1	Phase 2	Phase 3	Indication	Sponsor	Data Expected /Received
NCI-8871: Entinostat + *Tykerb* + *Herceptin*					HER2+ breast cancer	NCI[7]	December 2015
NCI-9253: Epigenetic Priming to Chemotherapy					NSCLC	NCI[8]	Second half of 2017

(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) This trial is in the planning phase and as such an IND has not yet been filed.
(3) Conducted pursuant to an IND application, which was filed with the FDA by Johns Hopkins University on April 22, 2013.
(4) Conducted pursuant to an IND application, which was filed with the FDA by the NCI on November 6, 2000.
(5) Conducted pursuant to an IND application, which was filed with the FDA by the NCI on November 5, 2015.
(6) Conducted pursuant to an IND application, which was filed with the FDA by the NCI on October 24, 2013.
(7) Conducted pursuant to an IND application, which was filed with the FDA by the NCI on November 6, 2000.
(8) Conducted pursuant to an IND application, which was filed with the FDA by the NCI on February 28, 2013.

Our Strategy

We are focused on 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 PDL-1 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 PDL-1 inhibitor. Our approach is to conduct clinical trials in patients with tumor types that are known to be responsive to PD-1 or PDL-1 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, Merck KGaA and Pfizer. In our collaboration with Merck, we intend to evaluate the safety, tolerability and efficacy of combining entinostat with *Keytruda*, an approved anti-PD-1 therapy, in NSCLC and melanoma. In our collaboration with Genentech, we plan to evaluate the safety, tolerability

and efficacy of entinostat in combination with atezolizumab, Genentech's investigational monoclonal antibody targeting PDL-1, in patients with TNBC. In our collaboration with Merck KGaA and Pfizer, we plan to evaluate the safety, tolerability and preliminary efficacy of entinostat in combination with avelumab, an investigational monoclonal antibody targeting PDL-1, in patients with ovarian cancer. 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.*** 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 assuming that one or more of our Phase 1b/2 clinical trials are successful. We may also seek breakthrough therapy designation from the FDA depending on the magnitude of the clinical benefit observed. We plan to take a strategic approach with respect to the order in which we choose to pursue FDA approvals that 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.
- ***Continue to develop and obtain regulatory approval for entinostat in combination with hormone therapy in advanced HR+ 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. A 600 patient Phase 3 clinical trial testing *Aromasin* in combination with entinostat versus *Aromasin* in combination with a placebo in patients with advanced HR+ breast cancer is currently being conducted by the ECOG-ACRIN under sponsorship and funding support from the 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. 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.
- ***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. As such, we intend to continue leveraging the collective talent within our organization and network of advisors to guide our pipeline expansion and development plans and to enable the execution of our business strategy.

Our Entinostat Program

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 specificity enhances immune responses against cancer and is likely to lead to a better tolerability and combinability profile.

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 PDL-1 and programmed cell death protein ligand 2, or PDL-2, that block the ability of immune cells known as cytotoxic T cells to kill cancer cells. Antibodies that block PDL-1 or PDL-2 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.

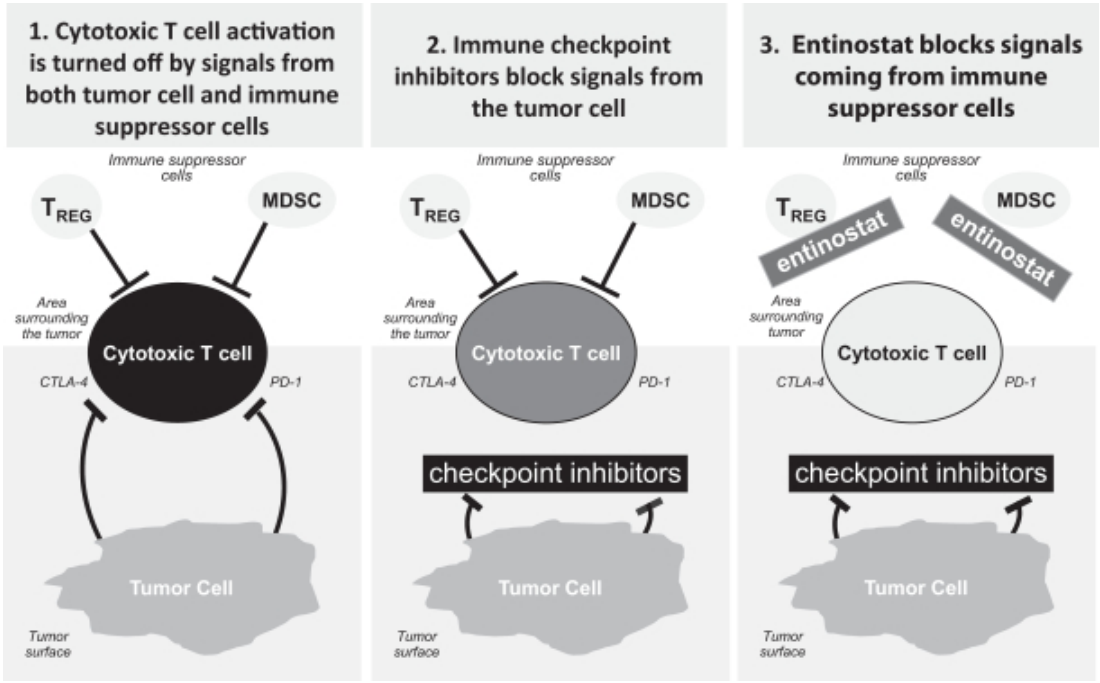
MDSCs are a group of immature myeloid cells that are activated by disease or injury and are generally increased in cancer patients. The primary function of MDSCs is to suppress an activated T cell immune response through the production and secretion of enzymes, which deplete key amino acids required 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 900 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.

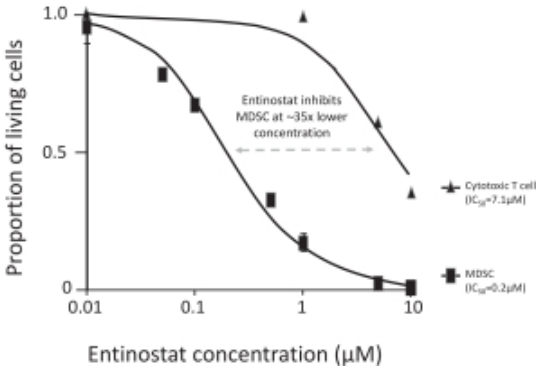
Figure 1.



Source: Syndax

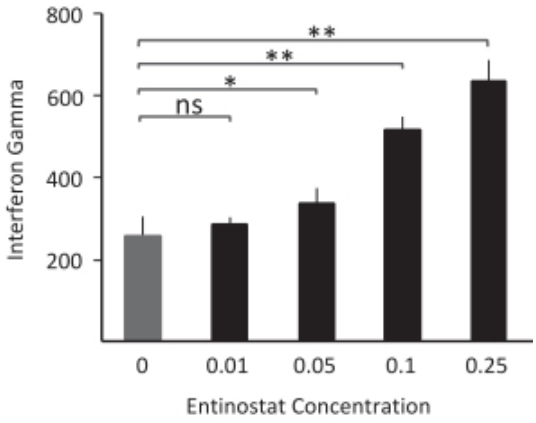
Data Supporting Entinostat as a Dual Inhibitor of Immune Suppressor Cells. Separate preclinical studies from investigators at Johns Hopkins University, or JHU, and Roswell Park Cancer Center have demonstrated that entinostat is a dual inhibitor of immune suppressor cells through its targeting of both 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: Adapted from Kim et al 2014 Proceedings of the National Academy of Sciences

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.

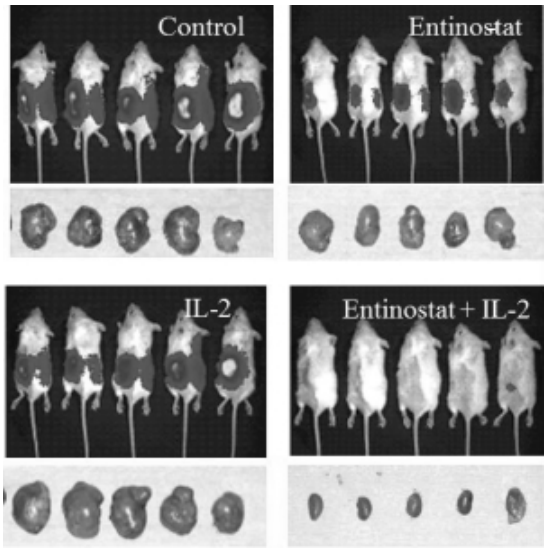
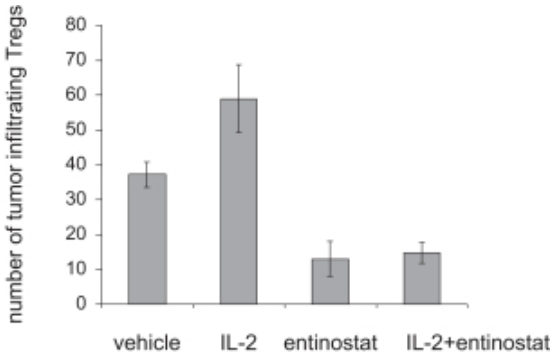
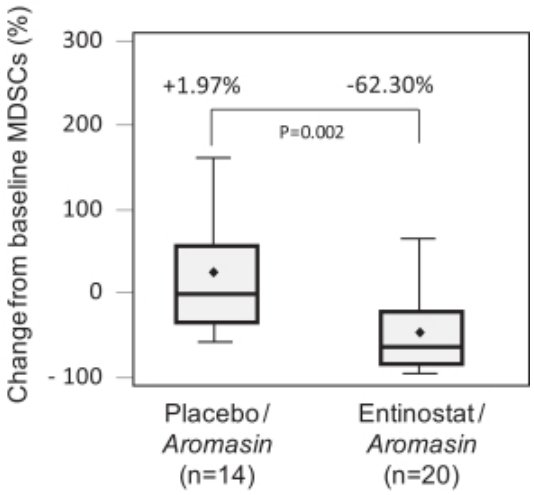


Figure 5.



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.

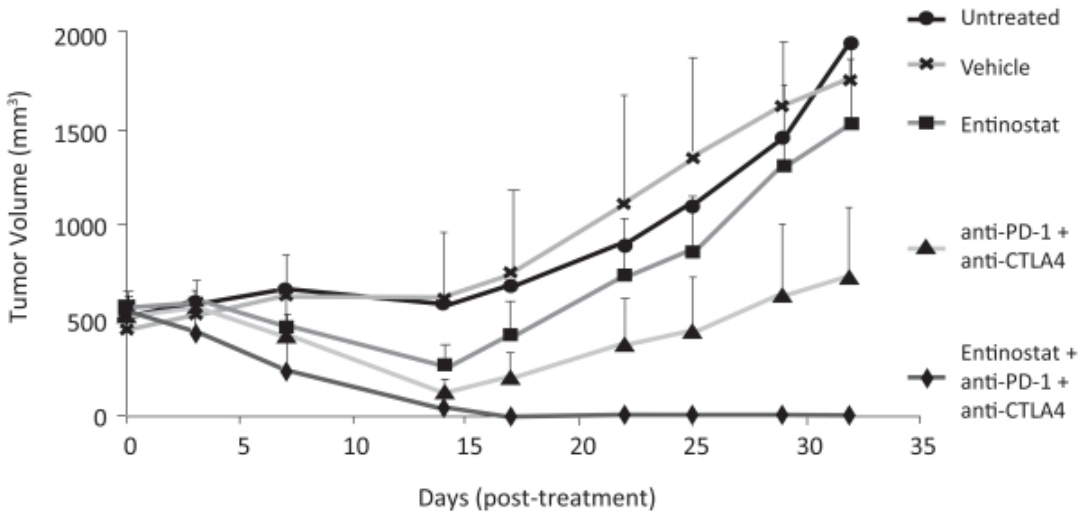


Source: Syndax

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 recently 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.

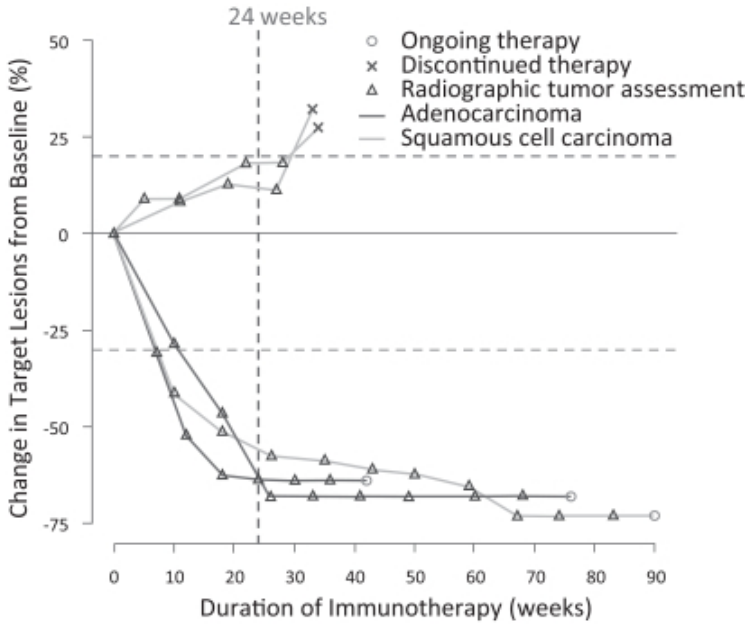
Figure 7.



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 PDL-1 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 PDL-1 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 85% to 90% of lung cancers are NSCLC, and in 2015, an estimated 221,200 new cases of lung cancer will be diagnosed and an estimated 158,040 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.

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 changed significantly in March 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. This approval was based on a trial that was stopped early after showing that *Opdivo* improved overall survival by 3.2 months compared to docetaxol, a comparator drug approved for this population. This data represents a significant increase in efficacy from what has traditionally been expected of drugs approved to treat advanced lung cancer, and we believe that immune checkpoint inhibitors will become the standard of care for this patient population. There are other immune checkpoint inhibitors being developed to treat NSCLC, the most advanced of which include Merck's *Keytruda*, Genentech's atezolizumab, AstraZeneca plc's MEDI4736, and Merck KGaA, Darmstadt, Germany/Pfizer Inc.'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 non-squamous, 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, the proportion of treated patients who respond is still quite low (15 to 20%). This low response rate leaves significant room to improve upon the benefit of immune checkpoint 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 6 to 10 months and the five-year survival rate for such patients is 16%. Although this rate has 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).

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. But, 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 established a clinical collaboration 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 designed as a Phase 1b/2 clinical trial. The Phase 1b portion will evaluate the safety, tolerability and biomarker correlates of the combination of entinostat and *Keytruda* in patients with NSCLC. The Phase 2 portion will assess 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. The trial will be conducted in the United States and will enroll up to 178 patients with approximately 42 of those in the Phase 1b portion and 136 of those in the Phase 2 portion. Patient enrollment for the Phase 1b portion of the clinical trial was initiated in August 2015. We expect safety data and RP2D data from the Phase 1b portion in the first half of 2016 and in the second half of 2016, respectively, and preliminary efficacy data from the Phase 2 portion in the first half of 2017. We anticipate that full enrollment for the Phase 1b and 2 portions will require approximately 30 months with final efficacy data expected in 2018.

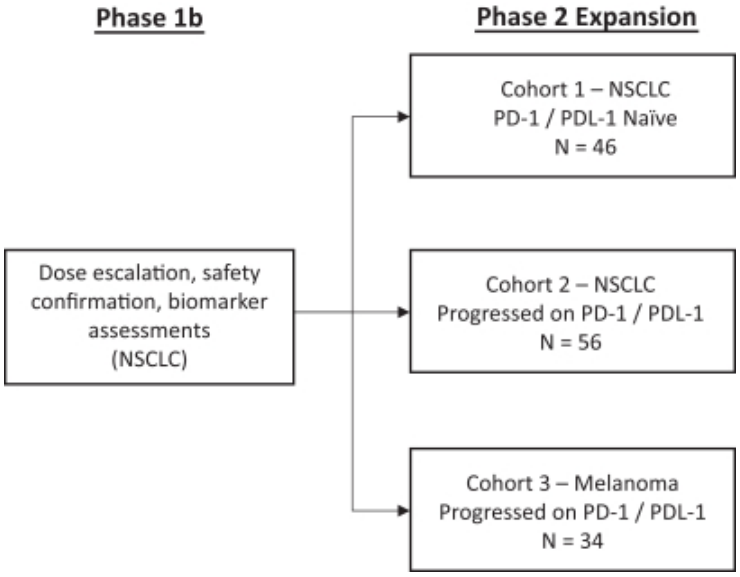
The primary objective of the Phase 1b portion of the trial is to determine the dose-limiting toxicities, or DLT, maximum tolerated dose, or MTD, or the RP2D of entinostat given in combination with *Keytruda*. The initial three patients in Cohort 1 received weekly oral entinostat at a starting dose of 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. Cohort 2 is currently enrolling. The prospective RP2D will be confirmed in 9 to 12 additional patients. The Phase 1b portion of the clinical trial is expected to also characterize the effect of the combination therapy on numerous biomarkers, including expression of PD-1 and PDL-1, the number and function of different types of T cells and the number of MDSCs. These biomarkers will be assessed both in peripheral blood and in serial tumor biopsies.

In the Phase 2 portion of the clinical trial, we will evaluate 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 a two-stage design will be used 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. The decision to terminate or continue enrollment for each cohort will be made independently of the other cohorts. Cohort 1 will enroll up to 46 NSCLC patients with any histology who have not previously been treated with a PD-1/PDL-1 inhibitor. We anticipate all 46 patients will be enrolled by the second half of 2017. 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 PDL-1 blocking antibody. We anticipate all 56 patients will be enrolled by the second half of 2017. Cohort 3 will enroll up to 34 patients with melanoma who have previously been treated and progressed on a PD-1 or PDL-1 blocking antibody. We anticipate all 34 patients will be enrolled by the first 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 2015 approximately 231,000 new cases of invasive breast cancer will be diagnosed 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 Genentech's atezolizumab results in approximately a 20% response rate in women with TNBC, and atezolizumab is currently being studied in a Phase 3 clinical trial.

Our Development Plan of Entinostat in TNBC. We have established a clinical collaboration with Genentech to study the safety and efficacy of entinostat in combination with atezolizumab, an anti-PDL-1 antibody, in patients with TNBC. The ENCORE 602 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 at a dose of 5 mg administered in combination with 1200 mg of atezolizumab given intravenously every three weeks. Assuming this combination is well tolerated, the Phase 2 portion of the clinical trial will be 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 entinostat activity on immune cells. We expect that the enrollment of patients in the ENCORE 602 clinical trial will begin during the first half of 2016 with data expected from the Phase 1b portion in the second half of 2016.

Entinostat with Immune Checkpoint Inhibitors in Ovarian Cancer

Market Overview and Current Treatment – Ovarian Cancer. A 2014 report by the American Cancer Society indicates that approximately 22,000 women are diagnosed and just over 14,000 die from ovarian cancer in the United States each year. 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 44% by 2009.

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. In 2014, two targeted agents were approved for later line treatment of refractory patients: *Avastin*® (bevacizumab), a vascular endothelial growth factor specific angiogenesis inhibitor, and *Lynparza*® (olaparib), a poly ADP-ribose polymerase inhibitor for patients with deleterious breast cancer susceptibility gene mutations. However, the duration of response to either drug 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.

Our Development Plan of Entinostat in Ovarian Cancer. We have established a clinical trial collaboration with Merck KGaA and Pfizer to study the safety and efficacy of entinostat in combination with avelumab, an investigational anti-PDL-1 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. We anticipate that enrollment of patients in the ENCORE 603 clinical trial will begin during the second half of 2016 with safety data expected from the Phase 1b portion in the first half of 2017 and RP2D data in the second half of 2017.

Additional Clinical Trials of Entinostat in Immuno-Oncology

We plan to evaluate the efficacy of entinostat in combination with other immune checkpoint inhibitors and/or other immunotherapies in at least one to two additional immuno-responsive tumor types. We expect to initiate these additional entinostat combination clinical trials in 2016.

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 three clinical trials that are designed to validate both clinical and preclinical observations that entinostat can enhance the clinical activity of immune therapy in patients. These clinical trials do not require additional financial support from us and are being conducted through our NCI collaboration with additional support from the *Stand Up To Cancer* funding initiative. Data from these trials are expected to be reported beginning in the second half of 2016. 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*. We expect efficacy data for this trial will be available from JHU in the second half of 2016.

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. As of December 2015, the Phase 2 portion of the trial has completed enrollment with 47 patients evaluable for safety and 39 evaluable for efficacy. Preliminary results of the entinostat—*Proleukin* combination in these patients were presented at the American Society of Clinical Oncology—Genitourinary meeting in January 2016 with data shown in Figures 9 and 10 below demonstrating a response rate of 35% (95% CI 20, 53%) in 37 patients with measurable disease and a median PFS of 16.1 months (95% CI 6.2, 27.8 months). The investigators concluded that the results suggest that entinostat may increase the anti-tumor activity of *Proleukin* by modulating immunosuppressive cells. It is expected that data pertaining to the overall response rate will be available in the first half of 2016.

Figure 9.

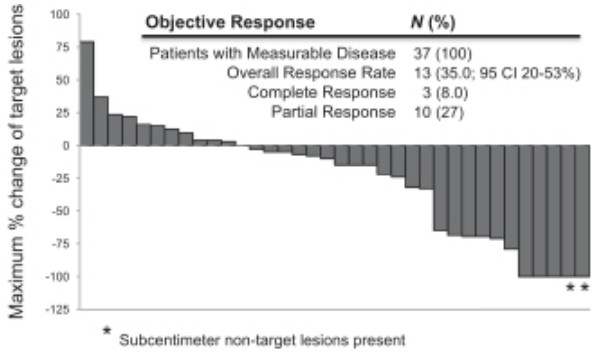
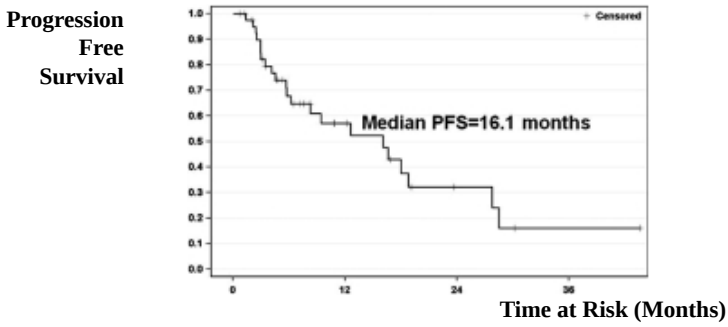


Figure 10.



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 is expected to begin 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 2012, approximately 42,000 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 2013, approximately 34,000 patients with HR+ breast cancer were treated with a hormone therapy as second-line 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*.

Recently 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.

Earlier this year the FDA granted accelerated approval to *Ibrance*® (palbociclib), a cyclin-dependent kinase 4 and 6 inhibitor 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. A recently reported Phase 3 clinical trial showed that the combination of *Ibrance* and *Faslodex* improved median PFS by approximately five months compared with *Faslodex* alone in women with HR+, HER2- breast cancer. Overall survival has not been reported for *Ibrance* clinical trials to date. However, based on the significant PFS benefit observed with *Ibrance*, we believe *Ibrance* will likely become the standard first-line therapy in this patient population either in combination with *Femara* or *Faslodex*.

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.

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

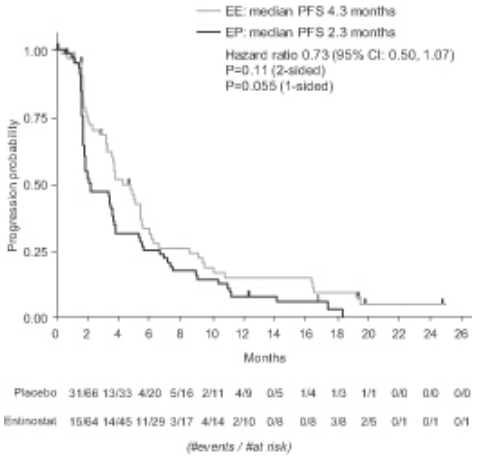
progressing on a non-steroidal aromatase inhibitor were randomly assigned to the combination of *Aromasin* (25 mg daily) and entinostat (5 mg once per week) or to the combination of *Aromasin* (25 mg daily) and a placebo. The primary endpoint was PFS, with overall survival as an exploratory endpoint.

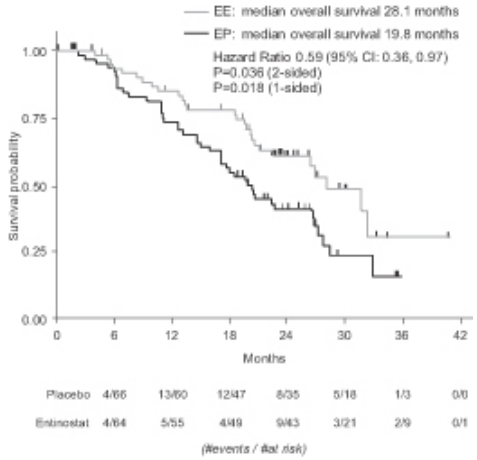
A Kaplan-Meier plot is a graphical statistical method commonly used to describe survival characteristics. The following are explanations of the meanings of the various efficacy endpoints that we have used in describing the results of our Phase 2b clinical trial. Each is determined in accordance with 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.

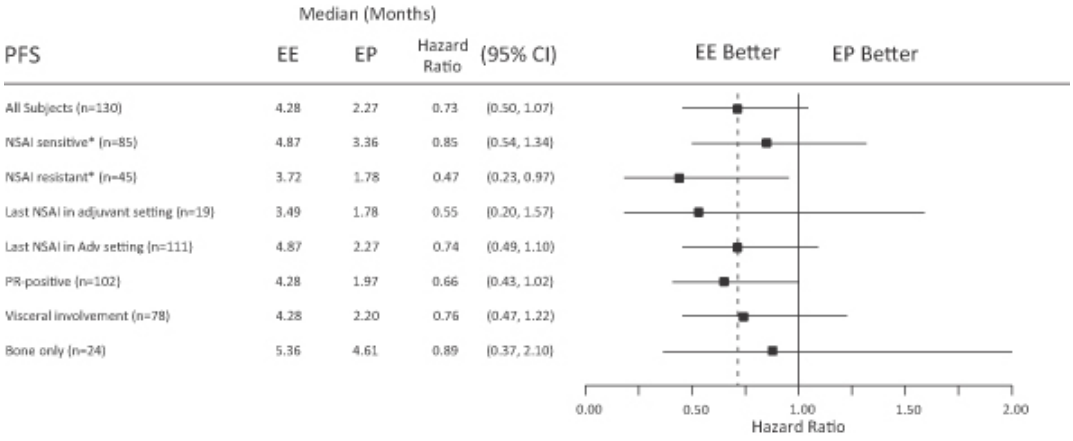
The trial met the statistical criteria for a positive PFS endpoint using a pre-specified p-value of 0.10 from a one-sided test for statistical significance. The overall survival benefit observed in the entinostat/*Aromasin* (exemestane tablets) (EE) group was also statistically significant versus the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

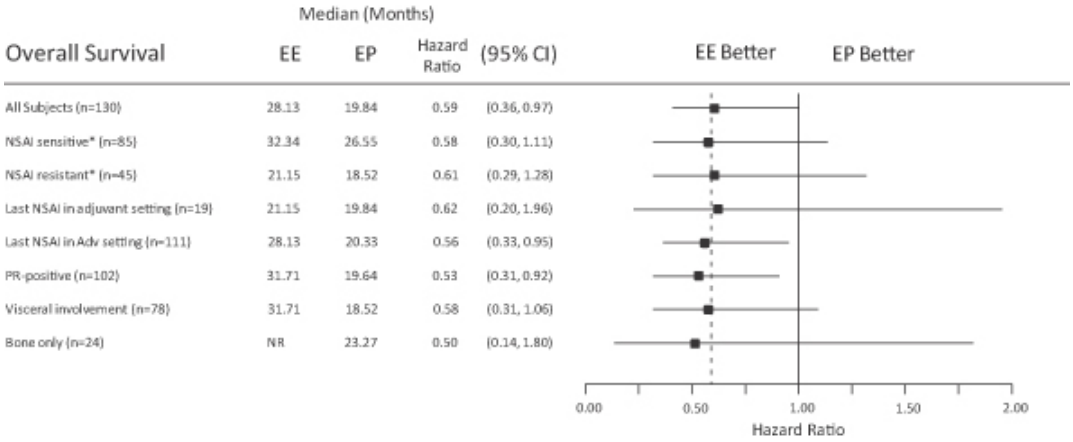
- Median PFS approximately doubled to 4.3 months in the EE group versus 2.3 months in the EP group, corresponding to a statistically significant hazard ratio of 0.73; 95% CI, 0.50 to 1.07; P2-sided=0.11; P1-sided=0.055.
- Median overall survival improved to 28.1 months in the EE group versus 19.8 months 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+ breast cancer.

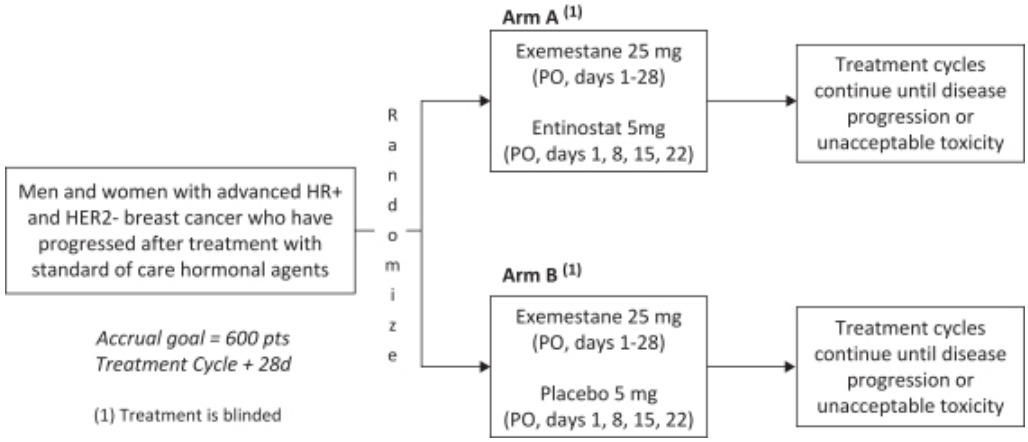
E2112: Ongoing Pivotal Phase 3 Clinical Trial

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 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 to be no sooner than 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 an 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 an NDA submission based on meeting the primary PFS endpoint.

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 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.

Additional Clinical Trials in Support of the NDA

In parallel with the pivotal Phase 3 clinical trial, we intend to conduct a number of required clinical pharmacology trials required for the submission of an 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 are pending. We will also conduct a Phase 1 clinical trial to determine whether entinostat interferes with the pharmacological properties of *Aromasin* (drug-drug interaction trial) and a Phase 1 clinical trial to confirm previous findings that there are no cardiac safety signals associated with entinostat treatment.

Collaborations

Clinical Collaborations in Immuno-Oncology

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, Inc.

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. We will share the study costs with Merck KGaA and Pfizer. 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

We have collaborated with a limited number of third parties on the clinical development of entinostat. For example, we have supplied entinostat for use in investigator-sponsored clinical trials conducted at JHU and we may 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. The investigator or institution generally also fully funds these clinical trials. To date, our sole obligation with respect to these investigator-sponsored clinical trials has been to supply entinostat for use in the trials. Additionally, we have an ongoing collaboration with the NCI for the clinical development of entinostat. As part of this collaboration, the NCI sponsors and funds clinical studies on entinostat that are conducted by other groups or institutions,

such as JHU and ECOG-ACRIN. Under a separate agreement with ECOG-ACRIN, we have agreed to make additional payments directly to ECOG-ACRIN to support its performance of an NCI-sponsored pivotal Phase 3 clinical trial of entinostat.

Collaborative Research and Development Agreement with the NCI

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

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

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

Either party may terminate the CRADA either by mutual consent or unilaterally upon advance written notice to the other party. Absent such early termination, the CRADA will expire on May 21, 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. Our aggregate payment obligations under this agreement are approximately $20.6 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.

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.

License Agreements

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 million in development and regulatory milestone payments and up to $25 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 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, 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 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 entinostat. 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+ 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, 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 also strive to protect entinostat with multiple layers of patents. As of February 26, 2016, our portfolio included six owned U.S. provisional patent applications, three owned pending U.S. non-provisional patent applications one granted non-U.S. patent and 13 non-U.S. pending patent applications. 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 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 applications relate to treatments with entinostat combined with anti PD-1 or anti PDL-1 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 November 2028 and June 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 August 24, 2015, the portfolio we licensed from Bayer included seven issued U.S. patents, 59 granted non-U.S. patents and 21 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 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 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 2029 expiration date.

Of the 59 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, 16 of the 21 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 2017, covers methods of treating selected cancers by administration of entinostat; U.S. Patent 7,687,525, which also expires in 2017, covers methods of treating autoimmune disease by administration of entinostat; U.S. Patent 6,320,078, which expires in 2019, covers methods of manufacturing entinostat; U.S. Patent No. 8,026,239, which expires in 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 2017, covers a subgenus of benzamide compounds that does not include entinostat; and U.S. Patent 6,794,392, which expires in 2017, covers a subgenus of benzamide compounds that does not include entinostat.

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 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 U.S. Patent and Trademark Office, or 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.

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 the 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 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 the NDA; and
- FDA review and approval of the 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. This process is known as a Special Protocol Assessment, or SPA. 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 the 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 the 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 the NDA submission is accepted for filing, the FDA reviews the 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 the 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 the 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 the NDA must submit a proposed REMS, and the FDA will not approve the 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 the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the 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 the 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. The 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 the 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 the 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, as amended by the Health Information Technology for Economic and Clinical Health Act, and their respective 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 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 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, imprisonment, exclusion from participation in government healthcare programs, 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, the President 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 Medicare Part B and Medicaid programs 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 beginning in 2014;
- 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. Data collection for these reporting requirements began on August 1, 2013, and manufacturers were required to submit reports to the U.S. Department of Health and Human Services by March 31, 2014. Beginning in 2015,

manufacturers are required to submit data reports by the 90th day of each calendar year. The U.S. Department of Health and Human Services discloses the information on a public website;

- 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.

Some of the reforms under the Affordable Care Act are slated for implementation in 2015. The effects of such reforms will be shaped significantly by implementing regulations that have yet to be finalized. In 2012, the Centers for Medicare and Medicaid Services, or CMS, issued proposed regulations to implement the changes to the Medicaid Drug Rebate Program under the ACA but has not yet issued final regulations. CMS is currently expected to release the final regulations later in 2015.

The Affordable Care Act also establishes an Independent Payment Advisory Board, or IPAB, to reduce the per capita rate of growth in Medicare spending. IPAB is mandated to propose recommendations to reduce the rate of Medicare spending growth if it is determined that the rate of growth of Medicare expenditures exceeds target growth rates. The IPAB has broad discretion to propose policies to reduce expenditures, which may have a negative impact on payment rates for medical products and services. A proposal made by the IPAB is required to be implemented by the U.S. government's Centers for Medicare and Medicaid Services unless Congress adopts a proposal intended to supersede the IPAB's recommendations or to discontinue the automatic implementation of the IPAB's proposals. IPAB proposals could impact payments for physician and free-standing services, among other things, beginning in 2015 and for hospital services beginning in 2020. However, as of early August 2015, the IPAB members have yet to be selected.

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 2024, which went into effect in April 2013. In January 2013, 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. 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 drugs 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 February 26, 2016, we had 19 full-time employees and one part-time employee. Of the full-time employees, ten were primarily engaged in research and development activities and five 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.

Facilities

Our headquarters is currently located in Waltham, Massachusetts, and consists of 4,712 square feet of leased office space under a lease that expires on April 30, 2017.

Legal Proceedings

We are not currently subject to any material legal proceedings.

MANAGEMENT

Directors and Executive Officers

The following table sets forth the name, age and position of each of our directors and executive officers as of February 26, 2016.

Name	Age	Position
Directors		
Dennis G. Podlesak(2)	58	Chairman of the Board of Directors
Henry Chen	45	Director
Fabrice Egros, Ph.D.(1)	53	Director
Luke Evnin, Ph.D.(2)(3)	52	Director
Kim P. Kamdar, Ph.D.(3)	48	Director
Ivor Royston, M.D.(3)	70	Director
Richard P. Shea(1)	64	Director
George W. Sledge Jr., M.D.(1)(2)	64	Director
Executive Officers		
Briggs W. Morrison, M.D.	56	Chief Executive Officer and Director
Michael A. Metzger.	45	President and Chief Operating Officer
Michael L. Meyers, M.D., Ph.D.	66	Senior Vice President, Chief Development Officer
Allan L. Shaw	52	Chief Financial Officer, Treasurer and Secretary
Peter Ordentlich, Ph.D.	47	Chief Technology Officer

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

The following includes a brief biography for each of our directors and executive officers. There are no family relationships among any of our directors or executive officers.

Directors

Dennis G. Podlesak has served as chairman of our board of directors since December 2008. Since November 2007, Mr. Podlesak has served as a partner at Domain Associates, LLC, a life science-focused venture capital firm. While at Domain, Mr. Podlesak has been the founder and the Chief Executive Officer of a number of companies, including Calixa Therapeutics, Inc., a privately held biopharmaceutical company which was acquired by Cubist Pharmaceuticals, Inc. in December 2009. Mr. Podlesak was also the Executive Chairman of Corthera, Inc., a privately held biopharmaceutical company, which was acquired by Novartis AG in January 2010. Prior to joining Domain, from 2005 to 2007, Mr. Podlesak served as the Founder and Chief Executive Officer of Cerexa, Inc., a privately held biotechnology company, which became a wholly owned subsidiary of Forest Laboratories, Inc. after being acquired by Forest in January 2007. From 2004 to 2005, Mr. Podlesak served as the Chief Executive Officer of Peninsula Pharmaceuticals Inc., a privately held pharmaceutical company, and in June 2005, he led the sale of Peninsula to Ortho-McNeil Pharmaceutical, Inc., a subsidiary of Johnson & Johnson. Prior to joining Peninsula, Mr. Podlesak held various senior executive positions at Novartis AG, a publicly traded healthcare company, Allergan plc, a publicly traded healthcare company, and SmithKline Beecham (now GlaxoSmithKline plc, a publicly traded pharmaceutical company). Mr. Podlesak currently serves on the board of Tobira Therapeutics, Inc., a publicly traded

biotechnology company, as well as on a number of private company boards. Until January 2015, Mr. Podlesak served on the board of Avanir Pharmaceuticals, Inc., a publicly traded biopharmaceutical company, until it was acquired by Otsuka Pharmaceuticals Co., Ltd. Mr. Podlesak received a B.A. and an M.B.A. from Pepperdine University, and has completed postgraduate studies at the Wharton School, University of Pennsylvania. We believe that Mr. Podlesak's experience in the venture capital industry, his experience as the Chief Executive Officer and Chairman of other successful companies in the biotechnology industry, his over 20 years of strategic, operational and commercial experience in the pharmaceutical industry, and his service as a director of other publicly traded and privately held life science companies give him the qualifications, skills and financial expertise to serve on our board of directors.

Henry Chen has served as a member of our board of directors since June 2015. Mr. Chen is the Managing Partner of Delos Capital Fund LP, a healthcare-focused venture capital fund. Prior to establishing Delos in 2014, Mr. Chen was a Partner and Co-Head of Asia at Permira Advisers LLP, a European private equity firm. Prior to joining Permira in 2008, Mr. Chen spent nine years in Investment Banking at Goldman Sachs & Co., where he was a Managing Director and co-headed the General Industrials Group, Asia (excluding Japan), which covered the consumer retail, healthcare, industrials and transportation sectors. Prior to that, Mr. Chen was a corporate finance lawyer with Davis Polk & Wardwell LLP in New York and Hong Kong. Mr. Chen received a B.A. and an M.A. from Harvard University and a J.D. from Harvard Law School. Mr. Chen's experience in the venture capital industry and his experience in the investment banking and legal industries give him the qualifications, skills and financial expertise to serve on our board of directors.

Fabrice Egros, Ph.D. has served as a member of our board of directors since September 2013. Since October 2015, Dr. Egros has served as President, Asia Pacific and Japan of Lupin Limited, an Indian publicly traded pharmaceutical company. From November 2012 to September 2015, Dr. Egros served as the Deputy Chief Executive Officer/Chief Operating Officer of NovaMedica LLC, a privately held pharmaceutical company, and was its Chief Operating Officer and a member of its board of directors from July 2012 to September 2015. From February 2011 to July 2012, Dr. Egros served as the Chief Operating Officer of Xanodyne Pharmaceuticals, Inc., a privately held pharmaceutical company. From September 2009 to February 2011, he served as the Senior Vice President, Corporate Business Development and Strategy of UCB, S.A., a publicly traded biopharmaceutical company. From August 2006 to August 2009, Dr. Egros served as the President of UCB, Inc., a subsidiary of UCB, S.A., and from September 2003 to August 2006, he served as the President of UCB Japan Co. Ltd., a subsidiary of UCB, S.A. Prior to joining UCB, Dr. Egros held various management and executive positions at Parke-Davis, Warner Lambert Company, a privately held pharmaceutical company, and Sanofi, formerly known as Sanofi-Aventis, a publicly traded pharmaceutical company. Dr. Egros received a B.S. in Pharmacokinetics and Metabolism from Schiller International University and a Pharm.D. and Ph.D. in Pharmaceutical Sciences from Chatenay Malabry University, and has participated in the Advanced Management Program at Harvard University. We believe that Dr. Egros's experience as an executive officer of other successful companies in the pharmaceutical industry gives him the qualifications, skills and financial expertise to serve on our board of directors.

Luke Evnin, Ph.D. has served as a member of our board of directors since May 2012. Dr. Evnin has served as a managing director at MPM Capital, a healthcare-focused venture capital firm, since he co-founded MPM's asset management business in 1997. Prior to joining MPM, Dr. Evnin spent seven years at Accel Partners, a venture capital firm, including four years as general partner. Dr. Evnin currently serves on a number of private company boards, and has served as director of several public companies, including Enteromedics Inc, Epix Medical, Inc., Intercell AG, Metabasis Therapeutics, Inc.

(acquired by Ligand Pharmaceuticals, Inc.), Oscient Pharmaceuticals Corp., Pacira Pharmaceuticals, Inc., Restore Medical, Inc. (acquired by Medtronic, Inc.), Sonic Innovations, Inc. and Signal Pharmaceuticals, Inc. (acquired by Celgene Corporation). Dr. Evnin received an A.B. in Molecular Biology from Princeton University and a Ph.D. in Biochemistry from the University of California, San Francisco. We believe that Dr. Evnin's experience in the venture capital industry and his service as a director of other publicly traded and privately held life science companies give him the qualifications, skill and financial expertise to serve on our board of directors.

Kim P. Kamdar, Ph.D. has served as a member of our board of directors since September 2006. Dr. Kamdar joined Domain Associates, LLC, a life science-focused venture capital firm, in January 2005 and has served as a partner at Domain since January 2011. Prior to joining Domain, Dr. Kamdar spent two years as a Kauffman Fellow with MPM Capital, Inc., a healthcare-focused venture capital firm. She also served as a Research Director at Novartis AG, a publicly traded healthcare company, and founded Aryzun Pharmaceuticals, Inc., a privately held biotechnology company. Dr. Kamdar currently serves as director of Neothetics, Inc, a publicly traded pharmaceutical company, and also serves on a number of private company boards. Dr. Kamdar received a B.A. from Northwestern University and a Ph.D. from Emory University. We believe that Dr. Kamdar's experience in the venture capital industry, and her service as a director of privately held life science companies give her the qualifications, skills and financial expertise to serve on our board of directors.

Ivor Royston, M.D. has served as a member of our board of directors since September 2013. In 1990, Dr. Royston founded Forward Ventures, a life science-focused venture capital firm, where he has served as a managing member. Since November 2014, Dr. Royston has served as Chief Executive Officer of Veracta, Inc., a privately held biotechnology company. Prior to founding Forward Ventures, Dr. Royston spent 10 years as the founding President and Chief Executive Officer of the Sidney Kimmel Cancer Center, a non-profit organization, and 12 years on the faculty of the medical school and cancer center at the University of California, San Diego. Dr. Royston also co-founded IDEC Corporation, which merged with Biogen, Inc. to form Biogen Idec, Inc. (now Biogen, Inc.), a publicly traded biotechnology company, and Hybritech, Inc., which was acquired by Eli Lilly & Company, a publicly traded company. Dr. Royston has served on a number of public and private company boards, and is currently a member of the board of directors of Biocept, Inc., a publicly traded molecular cancer diagnostic company, and MMRGlobal, Inc., a publicly traded health record company. Dr. Royston received a B.A. in Human Biology and an M.D. from Johns Hopkins University, and has completed post-doctoral training in Internal Medicine and Medical Oncology at Stanford University. We believe that Dr. Royston's experience in the venture capital industry, his experience co-founding other successful companies in the pharmaceutical industry, and his service as a director of other publicly traded and privately held life science companies give him the qualifications, skills and financial expertise to serve on our board of directors.

Richard P. Shea has served as a member of our board of directors since January 2014. Since July 2007, Mr. Shea has served as Senior Vice President and Chief Financial Officer of Momenta Pharmaceuticals Inc., a publicly traded biotechnology company, and has been its Vice President and Chief Financial Officer since October 2003. Prior to joining Momenta, he served as Chief Operating Officer and Chief Financial Officer of Variagenics Inc., a publicly traded pharmacogenomics company, that was merged with Hyseq Pharmaceuticals Inc., and as Vice President, Finance of Genetics Institute, Inc., a publicly traded biotechnology company, which was acquired by Wyeth Pharmaceuticals, Inc., which was then acquired by Pfizer, Inc. Mr. Shea is a certified public accountant and received an A.B. from Princeton University and an M.B.A. from the Public Management Program at Boston University. We believe that Mr. Shea's experience as an executive officer of other successful companies in the pharmaceutical industry gives him the qualifications, skills and financial expertise to serve on our board of directors.

George W. Sledge Jr., M.D. has served as a member of our board of directors since January 2014. Since January 2013, Dr. Sledge has been Professor and Chief of Medical Oncology at Stanford University Medical Center. Dr. Sledge served as a Co-director of the breast cancer program at the Indiana University Simon Cancer Center from 1989 to 2012, and was a Professor of Medicine and Pathology at the Indiana University School of Medicine from 1994 to 2013. From 2010 to 2011, Dr. Sledge served as the President of the American Society of Clinical Oncology, a professional organization representing oncologists. Dr. Sledge is currently Associate Editor of JAMA Oncology, and has served as a member of the External Advisory Committee for The Cancer Genome Atlas project, chairman of the Breast Committee of the Eastern Cooperative Oncology Group, chairman of the Education Committee of the American Society of Clinical Oncology, a member of the Department of Defense Breast Cancer Research Program's Integration Panel, and a member of the Food and Drug Administration's Oncology Drug Advisory Committee, and the NCI's Clinical Trials Advisory Committee. Dr. Sledge received a B.A. from the University of Wisconsin and an M.D. from Tulane University. We believe that Dr. Sledge's experience in the study and treatment of breast cancer and new drug development, his regulatory experience, and his experience as an executive officer of a professional organization gives him the qualifications, skills and financial expertise to serve on our board of directors.

Executive Officers

Briggs W. Morrison, M.D. has served as our Chief Executive Officer since June 2015 and as a member of our board of directors since July 2015. Dr. Morrison currently serves as a managing director of MPM Capital, a healthcare-focused venture capital firm, since June 2015. Prior to joining us, he served as Executive Vice President, Global Medicines Development and Chief Medical Officer at AstraZeneca plc, a publicly traded company, from January 2012 to June 2015, leading the company's global, late-stage development organization and serving as a member of the AstraZeneca senior executive team. He previously held a number of positions at Pfizer Inc., a publicly traded company, from 2007 to January 2012 that culminated in his appointment as Head, Medical Affairs, Safety and Regulatory Affairs for Pfizer's human health business, and also served in roles of increasing responsibility at Merck Research Laboratories, a division of Merck & Co., Inc., from 1995 to 2007, ascending to the role of Vice President, Clinical Sciences, Oncology, responsible for clinical development of all novel anti-cancer drugs. Dr. Morrison was chairman of the board of TransCelerate BioPharma Inc., an industry-funded company charged with improving aspects of clinical trials, from 2014 to 2015, a member of the executive committee of the Clinical Trials Transformation Initiative (CTTI) sponsored by FDA, and is on the board of ACRES (Alliance for Clinical Research Excellence and Safety). Dr. Morrison received a B.S. in biology from Georgetown University and an M.D. from the University of Connecticut. We believe that Dr. Morrison's experience as an executive officer of other successful companies in the pharmaceutical industry gives him the qualifications, skills and financial expertise to serve on our board of directors.

Michael A. Metzger has served as our President and Chief Operating Officer since May 2015. Prior to joining us, Mr. Metzger was President and COO from December 2013 to October 2014 and President and Chief Executive Officer and a member of the board of directors of Regado Biosciences, Inc., a former publicly traded company that merged with Tobira Therapeutics, Inc., from October 2014 to May 2015, where he oversaw the company's successful merger with Tobira Therapeutics, Inc. in 2015. Previously, Mr. Metzger served as Executive Vice President and Chief Operating Officer at Mersana Therapeutics, Inc., a privately held biopharmaceutical company developing novel immunoconjugate therapies for cancer, from March 2011 to November 2013, and in senior business development positions including leading mergers and acquisitions at Forest Laboratories, LLC, which

was acquired by Allergan plc, a publicly traded company, from 2006 to February 2011. Prior to Forest, Mr. Metzger served as Vice President Corporate Development at Onconova Therapeutics, Inc., from 2001 until 2006, and was a Managing Director at MESA Partners, Inc., a venture capital firm, from 1997 to 2001. Mr. Metzger received a B.A. from George Washington University and an M.B.A. in Finance from the New York University Stern School of Business.

Michael L. Meyers, M.D., Ph.D. has served as our Senior Vice President, Chief Development Officer since August 2015. Prior to joining us, Dr. Meyers held a number of senior roles at Johnson & Johnson, a publicly traded company, serving as Vice President, GU Oncology, Compound and Clinical Leader, and as Vice President, Oncology Scientific Innovation in Johnson and Johnson's London Innovation Centre. Dr. Meyers also led the U.S. Oncology Medical Affairs team at Aventis Pharmaceuticals Inc., a privately held life sciences company, predecessor to Sanofi-Aventis U.S. LLC, and worked in oncology clinical development at the Schering-Plough Research Institute. Dr. Meyers served on the Memorial Sloan Kettering Cancer Center faculty, specializing in Clinical Immunology and melanoma. He received his M.D. and his Ph.D. in Microbiology and Immunology from Albert Einstein College of Medicine in New York and was elected to the American Osteopathic Association. Dr. Meyers completed his residency in Internal Medicine at Columbia Presbyterian Medical Center and his fellowship, where he served as Chief Fellow in Medical Oncology, at Memorial Sloan Kettering Cancer Center.

Allan L. Shaw has served as our Chief Financial Officer, Treasurer and Secretary since January 2016. Prior to joining us, Mr. Shaw served as a Managing Director of Alvarez & Marsal LLC, a global professional services firm, and led their biopharmaceutical consulting practice, from December 2011 to March 2015, and supported Alvarez & Marsal LLC on an ad hoc basis from March 2015 to October 2015. Previously, Mr. Shaw served as the Chief Financial Officer of NewLead Holdings LTD., a publicly traded global shipping company, from 2009 to 2011. Mr. Shaw was the founder and Senior Managing Director of Shaw Strategic Capital LLC, an international financial advisory firm focused on providing strategic financial counsel on a wide variety of issues such as general corporate finance, mergers and acquisitions, capital structuring, licensing and capital markets, from 2005 to 2009. Prior to that, Mr. Shaw was the Chief Financial Officer of Serono S.A., a publicly traded global biotechnology company from 2002 to 2005. Mr. Shaw currently serves on the board of directors of Vivus Inc., a publicly traded biopharmaceutical company, Akari Therapeutics, Plc. (formerly Celsus Therapeutics), a publicly traded biopharmaceutical company, and Edith & Carl Marks JCH of Bensonhurst, a nonprofit organization. Mr. Shaw received a B.S. from the State University of New York (Oswego College) and is a certified public accountant in the State of New York.

Peter Ordentlich, Ph.D. co-founded the company in October 2005 and has served as our Chief Technology Officer since November 2013. Dr. Ordentlich previously served as our Vice President, Translational Medicine from January 2012 to October 2013, our Executive Director, Translational Science from January 2011 to December 2011, and our Director, Scientific Affairs and Strategic Alliances from January 2008 to December 2010. Prior to founding the company, Dr. Ordentlich was a scientist at the Salk Institute for Biological Studies, a biological research non-profit organization. He also spent five years as a research scientist at X-Ceptor Therapeutics, Inc., a drug discovery company, which was acquired by Exelixis, Inc. Dr. Ordentlich received a B.A. in Biochemistry and a Ph.D. in Immunology from the University of Pennsylvania.

Composition of the Board of Directors

Our amended and restated bylaws provide that the size of our board of directors will be determined from time to time by resolution of our board of directors. Our board of directors currently

consists of nine directors, seven of whom qualify as independent directors under the rules and regulations of the Securities and Exchange Commission, or SEC, and The NASDAQ Stock Market, LLC, or NASDAQ.

Election of Directors

Immediately prior to the completion of this offering, our amended and restated certificate of incorporation will provide for a classified board of directors consisting of three classes of directors. We will have three directors in each of Class I, Class II and Class III, each serving a staggered three-year term. At each annual meeting of stockholders, our stockholders will elect successors to directors whose terms then expire to serve from the time of election and qualification until the third annual meeting following election. After the completion of this offering, our directors will be divided among the three classes as follows:

- Class I directors will be Drs. Egros, Kamdar and Royston, and their terms will expire at the annual meeting of stockholders to be held in 2016;
- Class II directors will be Mr. Chen and Drs. Evnin and Sledge, and their terms will expire at the annual meeting of stockholders to be held in 2017; and
- Class III directors will be Dr. Morrison and Messrs. Podlesak and Shea, and their terms will expire at the annual meeting of stockholders to be held in 2018.

The classification of our board of directors may have the effect of delaying or preventing changes in control of our company. We expect that additional directorships resulting from an increase in the number of directors, if any, will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors.

Independence of the Board of Directors and Board Committees

Rule 5605 of the NASDAQ Marketplace Rules, or the NASDAQ Listing Rules, requires that independent directors compose a majority of a listed company's board of directors. In addition, the NASDAQ Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation, and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act of 1934, as amended, or the Exchange Act. Under NASDAQ Listing Rule 5605(a)(2), a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors or any other board committee: (1) accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries. In addition to satisfying general independence requirements under the NASDAQ Listing Rules, members of the compensation committee must also satisfy additional independence requirements set forth in NASDAQ Listing Rule 5605(d)(2). In order to be considered independent for purposes of NASDAQ Listing Rule 5605(d)(2), a member of a compensation committee of a listed company may not, other than in his or her capacity as a member of the compensation committee, the board of directors or any other board committee, accept, directly or indirectly, any consulting, advisory or other compensatory fee from the listed company or any of its

subsidiaries. Additionally, the board of directors of the listed company must consider whether the compensation committee member is an affiliated person of the listed company or any of its subsidiaries and, if so, must determine whether such affiliation would impair the director's judgment as a member of the compensation committee.

In August 2015, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family and other relationships, including those relationships described under "Certain Relationships and Related Party Transactions," our board of directors determined that none of our directors other than Dr. Morrison has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under Rule 5605(a)(2) of the NASDAQ Listing Rules. Dr. Morrison is not considered independent because he currently serves as our Chief Executive Officer. Our board of directors also determined that each member of the audit, compensation, and nominating and corporate governance committees satisfies the independence standards for such committees established by the SEC and the NASDAQ Listing Rules, as applicable. In making these determinations on the independence of our directors, our board of directors considered the relationships that each such non-employee director has with our company and all other facts and circumstances our board of directors deemed relevant in determining independence, including the beneficial ownership of our capital stock by each non-employee director.

Board Leadership Structure and the Role of the Board in Risk Oversight

Board Leadership Structure

The positions of our chairman of the board and Chief Executive Officer are separated. Separating these positions allows our Chief Executive Officer to focus on our day-to-day business, while allowing the chairman of the board to lead our board of directors in its fundamental role of providing advice to and independent oversight of management. Our board of directors recognizes the time, effort and energy that the Chief Executive Officer must devote to his position in the current business environment, as well as the commitment required to serve as our chairman, particularly as our board of directors' oversight responsibilities continue to grow. Our board of directors also believes that this structure ensures a greater role for the independent directors in the oversight of the company and active participation of the independent directors in setting agendas and establishing priorities and procedures for the work of our board of directors.

Although our amended and restated bylaws that will be in effect immediately prior to the completion of this offering will not require that we separate the chairman of the board and Chief Executive Officer positions, our board of directors believes that having separate positions is the appropriate leadership structure for us at this time. Our board of directors recognizes that depending on the circumstances, other leadership models, such as combining the role of chairman of the board with the role of Chief Executive Officer, might be appropriate. Accordingly, our board of directors may periodically review its leadership structure. Our board of directors believes its administration of its risk oversight function has not affected its leadership structure.

Our independent directors will meet alone in executive session at least quarterly each year. The purpose of these executive sessions is to promote open and candid discussion among the independent directors.

Role of the Board in Risk Oversight

We face a number of risks, including those described in the section titled "Risk Factors" contained elsewhere in this prospectus. Our board of directors believes that risk management is an important part of establishing, updating and executing on the company's business strategy. Our board of directors, as a whole and at the committee level, has oversight responsibility relating to risks that could affect the corporate strategy, business objectives, compliance, operations, and the financial condition and performance of the company. Our board of directors focuses its oversight on the most significant risks facing the company and on its processes to identify, prioritize, assess, manage and mitigate those risks. Our board of directors and its committees receive regular reports from members of the company's senior management on areas of material risk to the company, including strategic, operational, financial, legal and regulatory risks. While our board of directors has an oversight role, management is principally tasked with direct responsibility for management and assessment of risks and the implementation of processes and controls to mitigate their effects on the company.

The audit committee, as part of its responsibilities, oversees the company's significant financial and operational risk exposures, including but not limited to accounting matters, liquidity and credit risks, corporate tax positions, insurance coverage, and cash investment strategy and results. The audit committee is also responsible for overseeing the management of risks relating to the performance of the company's internal audit function (if required) and its independent registered accounting firm, as well as the company's systems of internal controls and disclosure controls and procedures. The compensation committee is responsible for overseeing the company's major compensation-related risk exposures, including risks related to executive compensation and overall compensation and benefit strategies, plans, arrangements, practices and policies. The nominating and corporate governance committee oversees the company's major legal compliance risk exposures, including the company's procedures and any related policies with respect to risk assessment and risk management. These committees provide regular reports to the full board of directors.

Committees of the Board

Our board of directors has a standing audit committee, compensation committee and nominating and corporate governance committee. The composition and responsibilities of each committee are described below. Members serve on these committees until their resignation or until otherwise determined by our board of directors.

Audit Committee

The audit committee is responsible for assisting our board of directors in its oversight of the integrity of our financial statements, the qualifications and independence of our independent auditors, and our internal financial and accounting controls. The audit committee has direct responsibility for the appointment, compensation, retention (including termination) and oversight of our independent auditors, and our independent auditors report directly to the audit committee. The audit committee also prepares the audit committee report that the SEC requires to be included in our annual proxy statement.

The members of the audit committee are Mr. Shea and Drs. Egros and Sledge, and Mr. Shea serves as chair of the audit committee. Each member of the audit committee qualifies as an independent director under the corporate governance standards of the NASDAQ Listing Rules and the independence requirements of Rule 10A-3 of the Exchange Act. Our board of directors has determined that Mr. Shea qualifies as an "audit committee financial expert" as such term is currently defined in

Item 407(d)(5) of Regulation S-K. The audit committee has adopted a written charter that satisfies the applicable standards of the SEC and the NASDAQ Listing Rules, which we will post on our website upon completion of this offering.

Compensation Committee

The compensation committee approves the compensation objectives for the company, approves the compensation of the Chief Executive Officer and approves or recommends to our board of directors for approval the compensation for other executives. The compensation committee reviews all compensation components, including base salary, bonus, benefits and other perquisites.

The members of the compensation committee are Drs. Evnin and Sledge and Mr. Podlesak, and Dr. Evnin serves as chair of the compensation committee. Each member of the compensation committee is a non-employee director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act and an outside director as defined by Section 162(m) of the U.S. Internal Revenue Code of 1986, as amended, or the Code, and each is an independent director as defined by the NASDAQ Listing Rules, including NASDAQ Listing Rule 5605(d)(2). The compensation committee has adopted a written charter that satisfies the applicable standards of the SEC and the NASDAQ Listing Rules, which we will post on our website upon completion of this offering.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee is responsible for making recommendations to our board of directors regarding candidates for directorships and the structure and composition of our board and the board committees. In addition, the nominating and corporate governance committee is responsible for developing and recommending to our board corporate governance guidelines applicable to the company and advising our board on corporate governance matters.

The members of the nominating and corporate governance committee are Drs. Evnin, Kamdar and Royston, and Dr. Kamdar serves as chair of the nominating and corporate governance committee. Each member of the nominating and corporate governance committee is a non-employee director within the meaning of Rule 16b-3 of the rules promulgated under the Exchange Act, and each is an independent director as defined by the NASDAQ Listing Rules. The nominating and corporate governance committee has adopted a written charter that satisfies the applicable standards of the NASDAQ Listing Rules, which we will post on our website upon completion of this offering.

Code of Business Conduct and Ethics

We adopted a code of business conduct and ethics that applies to all of our employees, officers and directors including those officers responsible for financial reporting. Upon completion of this offering, we will post the code of business conduct and ethics on our website. We intend to disclose future amendments to the code or any waivers of its requirements on our website to the extent permitted by the applicable rules and exchange requirements.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has ever been an officer or employee of the company. None of our executive officers serves, or has served during the last three years, as a member of our board of directors, compensation committee or other board committee performing equivalent functions of any entity that has one or more executive officers serving as one of our directors or on our compensation committee.

EXECUTIVE AND DIRECTOR COMPENSATION

Executive Compensation

Summary Compensation Table

The following table sets forth information for each of the last two completed fiscal years regarding compensation awarded to or earned by our named executive officers.

Name and Principal Position	Year	Salary ($)	Bonus[1] ($)	Option Awards[2] ($)	Other ($)	Total ($)
Briggs W. Morrison, M.D.[3] *Chief Executive Officer and Director*	2015	263,784	109,635	4,259,602	—	4,633,021
Michael A. Metzger[4] *President and Chief Operating Officer*	2015	296,538	50,000	2,550,157	—	2,896,695
Michael L. Meyers, M.D., Ph.D.[5]	2015	140,625	—	1,205,972	4,463[6]	1,351,060
Arlene M. Morris[7]	2015	162,231	—	—	656,592[8]	818,823
Former President and Chief Executive Officer	2014	424,360	144,282	394,967[9]	—	963,609

(1) The amounts paid to Dr. Morrison and Mr. Metzger during 2015 reflect signing bonuses paid to each executive at their time of hire. The bonus payments to our executive officers for 2015 have not yet been determined. We expect that they will be determined in the first quarter of 2016. The amount reflected for Ms. Morris for 2014 includes amounts earned in 2014, which were paid during 2015, based on the achievement of company and individual performance goals and other factors deemed relevant by our board of directors and compensation committee. For 2014, the compensation committee determined that Ms. Morris was entitled to approximately 85% of her target bonus.

(2) Amounts reflect the grant date fair value of option awards determined in accordance with ASC 718. For information regarding assumptions underlying the value of equity awards, see Note 12 to our audited consolidated financial statements and the discussion under the section titled “Management’s Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies—Stock-Based Compensation,” included elsewhere in this prospectus. These amounts do not correspond to the actual value the named executive officer may realize upon exercise of these option awards.

(3) Dr. Morrison joined the company on June 22, 2015.

(4) Mr. Metzger joined the company on May 5, 2015.

(5) Dr. Meyers joined the company on August 17, 2015.

(6) Amount reflects a benefits reimbursement.

(7) Ms. Morris resigned from the company effective May 12, 2015.

(8) Amount reflects the severance payment and payout of accrued vacation upon Ms. Morris’ resignation from the company.

(9) Includes the grant date fair value in the amount of $272,414 for option grants that were subsequently cancelled and reissued pursuant to an option exchange program that we implemented in 2014.

Outstanding Equity Awards at Fiscal Year-End

The following table provides information regarding equity awards held by the named executive officers that were outstanding as of December 31, 2015.

	Option Awards			
Name	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($/Sh)	Option Expiration Date
Briggs W. Morrison, M.D.	262,178[1]	—	10.90	9/9/2025
	548,223[1]	—	7.20	6/30/2025

Name	Option Awards: Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($/Sh)	Option Expiration Date
Michael A. Metzger	157,307(2)	—	10.90	9/9/2025
	328,933(2)	—	7.20	6/1/2025
Michael L. Meyers, M.D., Ph.D.	52,400(3)	—	10.90	9/9/2025
	109,679(3)		7.20	8/18/2025
		—		
Arlene M. Morris	25,667(4)	—	6.35	12/18/2024
	54,601(4)	—	6.32	9/15/2024
	228,285(4)	—	3.08	5/9/2023

(1) 37.5% of this option will vest upon the earlier of (i) June 22, 2016, the one year anniversary of the vesting commencement date, and (ii) the completion of this offering. Thereafter, the remainder will vest in equal monthly installments on the last day of each month over a three-year period of continuous service. This option is immediately exercisable. Shares of common stock issued upon exercise of an unvested option that has been "early exercised" are subject to the company's right of repurchase within 90 days of termination of employment.

(2) 37.5% of this option will vest upon the earlier of (i) May 5, 2016, the one year anniversary of the vesting commencement date, and (ii) the completion of this offering. Thereafter, the remainder will vest in equal monthly installments on the last day of each month over a three-year period of continuous service. This option is immediately exercisable. Shares of common stock issued upon exercise of an unvested option that has been "early exercised" are subject to the company's right of repurchase within 90 days of termination of employment.

(3) 25% of this option will vest on August 17, 2016, the one year anniversary of the vesting commencement date. Thereafter, the remainder will vest in equal monthly installments on the last day of each month over a three-year period of continuous service. This option is immediately exercisable. Shares of common stock issued upon exercise of an unvested option that has been "early exercised" are subject to the company's right of repurchase within 90 days of termination of employment.

(4) In accordance with our general release and post-separation consulting agreement with Ms. Morris, all of her options fully vested as of May 14, 2015. The outstanding options expire on January 14, 2017.

Employment Agreements

Below are descriptions of our offer letters and severance arrangements with our former executive officers as well as new employment agreements with certain of our current executive officers.

Current Executive Officers

Briggs W. Morrison, M.D. We entered into a new employment agreement with Briggs W. Morrison, M.D. that becomes effective on the date of effectiveness of the registration statement of which this prospectus is a part. Dr. Morrison's employment agreement provides for his at-will employment as our Chief Executive Officer. Dr. Morrison's annual base salary is $501,000, which may be increased from time to time based on the review by our compensation committee. Upon the completion of this offering, Dr. Morrison's annual base salary will be increased to $531,000. Dr. Morrison's employment agreement further provides that he is eligible to earn an annual target performance bonus of up to 40% of his annual base salary upon attainment of objectives to be determined by our board of directors or our compensation committee, which bonus for the 2015 calendar year, if applicable, will be pro-rated based on Dr. Morrison's start date with us. Upon the completion of this offering, Dr. Morrison will be eligible to receive a one-time bonus equal to $100,000.

Pursuant to his employment agreement, Dr. Morrison also is entitled to reimbursement for all necessary and reasonable business expenses incurred in connection with his duties in accordance with our generally applicable policies. Additionally, we have agreed to reimburse, or pay for, all reasonable

expenses incurred by Dr. Morrison in connection with commuting between our Waltham office and his current principal residence, including Dr. Morrison's actual and reasonable living expenses incurred in the Waltham area and his current principal residence. If Dr. Morrison decides to relocate his residence to Waltham, we have agreed to pay Dr. Morrison for ordinary and necessary expenses incurred by him as a result of his relocation.

Dr. Morrison's employment agreement further provides that in the event his employment is terminated without "cause," as defined in his employment agreement, or he terminates his employment for "good reason," as defined in his employment agreement, he is entitled to (i) a lump sum severance payment equal to 12 months base salary, (ii) a portion of his annual target performance bonus in effect as of the termination based on the number of days Dr. Morrison was employed in the year of termination, (iii) payment on his behalf of up to 18 months of health insurance benefits continuation, (iv) with respect to equity awards granted to Dr. Morrison prior to the date of his termination, accelerated vesting and the lapse of any reacquisition or repurchase rights we hold with respect to such equity awards for the portion of such equity awards that would have otherwise vested within the 12-month period following the date of Dr. Morrison's termination of employment without cause or for good reason were he to remain employed with us during such 12-month period and (v) an extension on the time period during which Dr. Morrison has to exercise any options that are held by him on the date of his termination of employment to the shorter of (A) 12 months or (B) the remaining term of the option. If Dr. Morrison's employment is terminated without cause or he terminates his employment for good reason within three months prior to or 12 months after a "change in control," as defined in his employment agreement, he is instead entitled to (a) a lump sum severance payment equal to the sum of 12 months base salary and 100% of the greater of (1) the average annual target performance bonus paid to him for the preceding three years or (2) his annual target performance bonus in effect as of the change in control, (b) payment on his behalf of up to 18 months of health insurance benefits continuation and (c) full accelerated vesting on all of his unvested options and the lapse of any reacquisition or repurchase rights we hold with respect to any other equity award granted to him pursuant to any of our equity incentive plans and (d) an extension on the time period during which Dr. Morrison has to exercise any options that are held by him on the date of his termination of employment to the shorter of (A) 12 months or (B) the remaining term of the option. In order to receive his severance benefits, Dr. Morrison must sign a general release of claims. Dr. Morrison's employment agreement further provides that upon a "change in control," as defined in his employment agreement, with an aggregate purchase price of at least $640 million, Dr. Morrison will be eligible to receive an additional one-time bonus equal to his then current annual base salary.

In addition, Dr. Morrison's employment agreement provides that in the event the severance and other benefits provided for or otherwise payable to Dr. Morrison constitute "parachute payments" within the meaning of Section 280G of the Code and are subject to the excise tax imposed by Section 4999 of the Code, we will pay either (i) Dr. Morrison's severance benefits under the employment agreement in full or (ii) only a part of Dr. Morrison's severance benefits under the employment agreement such that Dr. Morrison receives the largest payment possible without the imposition of the excise tax, in each case, depending upon which alternative would result in Dr. Morrison receiving the greater net after-tax payment.

Michael A. Metzger. We entered into a new employment agreement Michael A. Metzger that becomes effective on the date of effectiveness of the registration statement of which this prospectus is a part. Mr. Metzger's employment agreement provides for his at-will employment as our President and Chief Operating Officer. Mr. Metzger's annual base salary is $450,000, which may be increased from time to time based on the review by our compensation committee. Upon the completion of this

offering, Mr. Metzger's annual base salary will be increased to $475,000. Mr. Metzger's employment agreement further provides that he is eligible to earn an annual target performance bonus of up to 40% of his annual base salary upon attainment of objectives to be determined by our board of directors or our compensation committee, which bonus for the 2015 calendar year, if applicable, will be pro-rated based on Mr. Metzger's start date with us. Upon the completion of this offering, Mr. Metzger will be eligible to receive a one-time bonus equal to $40,000.

Pursuant to his employment agreement, Mr. Metzger also is entitled to reimbursement for all necessary and reasonable business expenses incurred in connection with his duties in accordance with our generally applicable policies. Additionally, we have agreed to reimburse, or pay for, all reasonable expenses incurred by Mr. Metzger in connection with commuting between our Waltham office and his current principal residence, including Mr. Metzger's actual and reasonable living expenses incurred in the Waltham area and his current principal residence. If Mr. Metzger decides to relocate his residence to Waltham, we have agreed to pay Mr. Metzger up to $50,000 for ordinary and necessary expenses incurred by him as a result of his relocation.

Mr. Metzger's employment agreement further provides that in the event his employment is terminated without "cause," as defined in his employment agreement, or he terminates his employment for "good reason," as defined in his employment agreement, he is entitled to (i) a lump sum severance payment equal to 12 months base salary, (ii) a portion of his annual target performance bonus in effect as of the termination based on the number of days Mr. Metzger was employed in the year of termination, (iii) payment on his behalf of up to 18 months of health insurance benefits continuation, (iv) with respect to equity awards granted to Mr. Metzger prior to the date of his termination, accelerated vesting and the lapse of any reacquisition or repurchase rights we hold with respect to such equity awards for the portion of such equity awards that would have otherwise vested within the 12-month period following the date of Mr. Metzger's termination of employment without cause or for good reason were he to remain employed with us during such 12-month period and (v) an extension on the time period during which Mr. Metzger has to exercise any options that are held by him on the date of his termination of employment to the shorter of (A) 12 months or (B) the remaining term of the option. If Mr. Metzger's employment is terminated without cause or he terminates his employment for good reason within three months prior to or 12 months after a "change in control," as defined in his employment agreement, he is instead entitled to (a) a lump sum severance payment equal to the sum of 12 months base salary and 100% of the greater of (1) the average annual target performance bonus paid to him for the preceding three years or (2) his annual target performance bonus in effect as of the change in control, (b) payment on his behalf of up to 18 months of health insurance benefits continuation and (c) full accelerated vesting on all of his unvested options and the lapse of any reacquisition or repurchase rights we hold with respect to any other equity award granted to him pursuant to any of our equity incentive plans and (d) an extension on the time period during which Mr. Metzger has to exercise any options that are held by him on the date of his termination of employment to the shorter of (A) 12 months or (B) the remaining term of the option. In order to receive his severance benefits, Mr. Metzger must sign a general release of claims. Mr. Metzger's employment agreement further provides that upon a "change in control," as defined in his employment agreement, with an aggregate purchase price of at least $640 million, Mr. Metzger will be eligible to receive an additional one-time bonus equal to his then current annual base salary.

In addition, Mr. Metzger employment agreement provides that in the event the severance and other benefits provided for or otherwise payable to Mr. Metzger constitute "parachute payments" within the meaning of Section 280G of the Code and are subject to the excise tax imposed by Section 4999 of the Code, we will pay either (i) Mr. Metzger's severance benefits under the

employment agreement in full or (ii) only a part of Mr. Metzger's severance benefits under the employment agreement such that Mr. Metzger receives the largest payment possible without the imposition of the excise tax, in each case, depending upon which alternative would result in Mr. Metzger receiving the greater net after-tax payment.

Michael L. Meyers, M.D., Ph.D. We entered into a new employment agreement with Michael L. Meyers M.D., Ph.D. that becomes effective on the date of effectiveness of the registration statement of which this prospectus is a part. Dr. Meyers' employment agreement provides for his at-will employment as our Senior Vice President, Chief Development Officer. Pursuant to Dr. Meyers' employment agreement, Dr. Meyers' annual base salary is $375,000, and may be increased from time to time based on the review of our compensation committee. Dr. Meyers' employment agreement further provides that he is eligible to earn an annual target performance bonus of up to 35% of his annual base salary upon attainment of objectives to be determined by our board of directors or our compensation committee, which bonus for the 2015 calendar year, if applicable, will be pro-rated based on Dr. Meyers' start date with us. Dr. Meyers also is entitled to reimbursement for all necessary and reasonable business expenses incurred in connection with his duties in accordance with our generally applicable policies.

Dr. Meyers' employment agreement further provides that in the event his employment is terminated without "cause," as defined in his employment agreement, or he terminates his employment for "good reason," as defined in his employment agreement, he is entitled to (i) a lump sum severance payment equal to six months base salary and (ii) payment on his behalf of up to 12 months of health insurance benefits continuation. If Dr. Meyers' employment is terminated without cause or he terminates his employment for good reason within three months prior to or 12 months after a "change in control" of us, as defined in his employment agreement, he is instead entitled to (a) a lump sum severance payment equal to the sum of 12 months base salary and 100% of the greater of (1) the average annual target performance bonus paid to him for the preceding three years or (2) his annual target performance bonus in effect as of the change in control, (b) payment on his behalf of up to 12 months of health insurance benefits continuation and (c) full accelerated vesting on all of his unvested options and the lapse of any reacquisition or repurchase rights we hold with respect to any other equity award granted to him pursuant to any of our equity incentive plans. In order to receive his severance benefits, Dr. Meyers must sign a general release of claims.

In addition, Dr. Meyers' employment agreement provides that in the event the severance and other benefits provided for or otherwise payable to Dr. Meyers' constitute "parachute payments" within the meaning of Section 280G of the Code and are subject to the excise tax imposed by Section 4999 of the Code, we will pay either (i) Dr. Meyers' severance benefits under the employment agreement in full or (ii) only a part of Dr. Meyers' severance benefits under the employment agreement such that Dr. Meyers receives the largest payment possible without the imposition of the excise tax, in each case, depending upon which alternative would result in Dr. Meyers receiving the greater net after-tax payment.

Former Chief Executive Officer

Arlene M. Morris. We entered into an offer letter with Arlene M. Morris, our former President and Chief Executive Officer, in May 2012, which governed the terms of her at-will employment with us prior to her resignation in May 2015. Pursuant to the offer letter, Ms. Morris was entitled to an annual base salary of $400,000, which increased to $424,360 in 2014, and was eligible to receive an annual target performance bonus of up to 40% of her annual base salary upon attainment of objectives to be determined by our board of directors. Ms. Morris was entitled to reimbursement for all necessary

and reasonable business expenses incurred in connection with her duties in accordance with our generally applicable policies. Additionally, we agreed to reimburse, or pay for, all reasonable expenses incurred by Ms. Morris in connection with commuting between our Waltham office and her current principal residence, including Ms. Morris's actual and reasonable living expenses incurred in the Boston area and her actual and reasonable commuting expenses incurred between Waltham and her current principal residence, up to a maximum of $10,000 per month.

In connection with her resignation in May 2015, Ms. Morris entered into a general release and post-separation consulting agreement in May 2015. Pursuant to Ms. Morris' general release and post-separation consulting agreement and in consideration of providing us with consulting services through July 13, 2015, Ms. Morris received a consulting fee of approximately $36,425 per month for two months. Additionally, pursuant to Ms. Morris' separation agreement and post-separation consulting agreement (a) Ms. Morris received a lump sum payment equal to $437,090, which was an amount equal to 12 months of Ms. Morris' monthly base salary on the date of her termination, 60 days after her termination date, (b) Ms. Morris is entitled to receive a payment on her behalf of up to 12 months of health insurance benefits continuation, (c) all unvested options held by Ms. Morris on her termination date fully vested and Ms. Morris has the right to exercise such options until and including January 13, 2017 and (d) Ms. Morris received a lump sum bonus of $100,000 as a result of the closing of the Series C-1 financing, which was determined at the discretion of our board of directors. Ms. Morris also received $5,038 reimbursement of her legal fees incurred in connection with the negotiation of her separation agreement and post-separation consulting agreement.

Other Benefits

Our named executive officers are eligible to participate in all of our employee benefit plans, such as medical, dental, vision, group life, short and long-term disability and our 401(k) plan, in each case on the same basis as other employees, subject to applicable laws. We also provide vacation and other paid holidays to all employees, including our named executive officers. We believe these benefits are important to attracting and retaining experienced executives. Like many private companies, we do not currently provide perquisites to our executive officers, given our attention to the cost-benefit tradeoff of such benefits, and our board of directors' knowledge of the benefit offerings at other private companies.

Tax and Accounting Considerations

Section 162(m) of the Code generally disallows a tax deduction for compensation in excess of $1.0 million paid to our Chief Executive Officer and our three other most highly paid executive officers other than our principal financial officer. Qualifying performance-based compensation is not subject to the deduction limitation if specified requirements are met. We generally intend to structure the performance-based portion of our executive compensation, when feasible, to comply with exemptions in Section 162(m) so that the compensation remains tax deductible to us. However, our board of directors may, in its judgment, authorize compensation payments that do not comply with the exemptions in Section 162(m) when it believes that such payments are appropriate to attract and retain executive talent.

Our compensation committee also takes into account whether components of our compensation program may be subject to the penalty tax associated with Section 409A of the Code, and aims to structure the elements of compensation to be compliant with or exempt from Section 409A to avoid such potential adverse tax consequences.

In addition, we account for equity compensation paid to our employees in accordance with ASC 718, which requires us to estimate and record an expense over the service period of the award. We record cash compensation as an expense at the time the obligation is accrued. The accounting impact of our compensation programs is one of many factors that we consider in determining the size and structure of our programs.

Equity Benefit Plans

2015 Omnibus Incentive Plan

Our board of directors adopted the 2015 Plan in September 2015, and our stockholders approved the 2015 Plan in February 2016. The 2015 Plan will become effective upon completion of this offering. We believe adoption and maintenance of the 2015 Plan will help us attract and retain executive officers, other employees and service providers, as well as our non-employee directors. We believe that awarding grants to our executive officers and others will stimulate their efforts toward our continued success, long-term growth and profitability. The 2015 Plan will provide for the grant of stock options, stock appreciation rights, restricted stock, unrestricted stock, stock units, dividend equivalent rights, performance awards, annual incentive awards and other equity-based awards. We will reserve 1,750,000 shares of common stock (which includes 350,760 shares reserved for issuance under our 2007 Plan as of December 31, 2015) for issuance pursuant to the 2015 Plan, subject to certain adjustments set forth in the 2015 Plan. Any shares of common stock related to awards outstanding under the 2007 Plan upon completion of this offering, which 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. In addition, effective January 1, 2017 and continuing until the expiration of the 2015 Plan, the number of shares of common stock available for issuance under the 2015 Plan will automatically increase annually by an amount equal to the lesser of (i) 4% of the total number of issued and outstanding shares of our common stock as of December 31 of the immediately preceding year and (ii) the number of shares (which may be zero) as determined in the discretion of our board of directors by action taken prior to the beginning of that calendar year. A maximum of 1,750,000 shares of common stock reserved for issuance under the 2015 Plan will be available for issuance as incentive stock options. This summary is qualified in its entirety by the detailed provisions of the 2015 Plan, which is filed as an exhibit to the registration statement of which this prospectus is a part.

Section 162(m) of the Code limits publicly held companies to an annual deduction for U.S. federal income tax purposes of $1,000,000 for compensation paid to each of their Chief Executive Officer and their three highest compensated executive officers (other than the Chief Executive Officer and the principal financial officer) determined at the end of each year, who are referred to as covered employees. However, certain performance-based compensation is excluded from this limitation. The 2015 Plan is designed to permit the compensation committee to grant awards that qualify as performance-based compensation for purposes of satisfying the conditions of Section 162(m) of the Code, but the 2015 Plan does not require that awards qualify for this exemption.

Administration of the 2015 Plan

Our compensation committee will administer the 2015 Plan and determine all terms of awards under the 2015 Plan. Each member of our compensation committee who administers the 2015 Plan will be both a “non-employee director” within the meaning of Rule 16b-3 of the Exchange Act, and an “outside director” within the meaning of Section 162(m) of the Code. Our compensation committee

will also determine who will receive awards under the 2015 Plan, the type of award and its terms and conditions and the number of shares of our common stock subject to the award, if the award is equity-based. Our compensation committee will also interpret the provisions of the 2015 Plan. During any period of time in which we do not have a compensation committee, our board of directors or another committee appointed by our board of directors will administer the 2015 Plan. References below to the compensation committee include a reference to the board of directors or another committee appointed by the board of directors for those periods in which the board of directors or such other committee appointed by the board of directors is acting.

Eligibility

All of our employees and the employees of our affiliates will be eligible to receive awards under the 2015 Plan. In addition, our non-employee directors and consultants and advisors who perform services for us and our affiliates may receive awards under the 2015 Plan, other than incentive stock options.

Share Authorization

We reserved 1,750,000 shares of common stock for issuance under the 2015 Plan, which includes all shares of common stock that remain available for issuance under the 2007 Plan as of the completion of this offering. In connection with stock splits, dividends, recapitalizations and certain other events, our board of directors will make proportionate adjustments that it deems appropriate in the aggregate number of shares of common stock that we may issue under the 2015 Plan and the terms of outstanding awards. If any shares of stock covered by an award granted under the 2015 Plan or the 2007 Plan are not purchased or are forfeited or expire, or if an award otherwise terminates without delivery of any shares of stock subject thereto, or is settled in cash in lieu of shares of stock, then the number of shares of stock counted against the aggregate number of shares of stock available under the 2015 Plan with respect to such award will again be available for making awards under the 2015 Plan.

During any time that the transition period under Section 162(m) of the Code has expired or does not apply, the maximum number of shares of common stock subject to options or stock appreciation rights that we will be able to issue under the 2015 Plan to any person will be 437,500 in any single calendar year. The maximum number of shares of common stock that we will be able to issue under the 2015 Plan to any person other than pursuant to an option or stock appreciation right will be 218,750 in any single calendar year. The maximum amount that any one person may earn as a cash-denominated annual incentive award in any calendar year in respect of a performance period of 12 months or less will be $1,000,000 and the maximum amount that any one person may earn as a cash-denominated performance award in respect of a performance period greater than 12 months will be $3,000,000.

Options

The 2015 Plan will authorize our compensation committee to grant incentive stock options (under Section 421 of the Code) and options that do not qualify as incentive stock options, or non-qualified stock options. Our compensation committee will determine the exercise price of each option, provided that the price will be equal to at least the fair market value of the shares of common stock on the date on which the option is granted. If we were to grant incentive stock options to any 10% stockholder, the exercise price may not be less than 110% of the fair market value of our shares of common stock on the date of grant.

The term of an option cannot exceed 10 years from the date of grant. If we were to grant incentive stock options to any 10% stockholder, the term cannot exceed five years from the date of grant. The

compensation committee will determine at what time or times each option may be exercised and the period of time, if any, after retirement, death, disability or termination of employment during which options may be exercised. Options may be made exercisable in installments. The compensation committee may accelerate the exercisability of options. Except in connection with a corporate transaction involving us, our compensation committee may not, without stockholder approval, reduce the exercise price of an option after the grant of the option, cancel an outstanding option in exchange for or substitution of a new option having an exercise price below that of the option that was surrendered, or cancel an outstanding option with an exercise price above the current share price in exchange for cash or other securities.

The aggregate fair market value, determined at the time of grant, of our common stock with respect to incentive stock options that are exercisable for the first time by an optionee during any calendar year under all of our stock plans may not exceed $100,000. We will generally treat options or portions thereof that exceed such limit as non-qualified stock options.

Stock Appreciation Rights

The 2015 Plan will authorize our compensation committee to grant stock appreciation rights that provide the recipient with the right to receive, upon exercise of the stock appreciation right, cash, shares of common stock or a combination of the two. The amount that the recipient will receive upon exercise of the stock appreciation right generally will equal the excess of the fair market value of our common stock on the date of exercise over the shares' fair market value on the date of grant. Stock appreciation rights will become exercisable in accordance with terms determined by our compensation committee. Stock appreciation rights may be granted in tandem with an option grant or independently from an option grant. The term of a stock appreciation right cannot exceed 10 years from the date of grant.

Stock Awards

The 2015 Plan will also provide for the grant of stock awards (which includes restricted stock and unrestricted stock). A stock award is an award of shares of common stock that may be subject to restrictions on transferability and other restrictions as our compensation committee determines in its sole discretion on the date of grant. The restrictions, if any, may lapse over a specified period of time or through the satisfaction of conditions, in installments or otherwise, as our compensation committee may determine. A participant who receives a restricted stock award will have all of the rights of a stockholder as to those shares, including the right to vote and the right to receive dividends or distributions on the shares, except that the board of directors may require any dividends to be reinvested in shares. During the period, if any, when stock awards are non-transferable or forfeitable, a participant is prohibited from selling, transferring, assigning, pledging or otherwise encumbering or disposing of his or her award shares.

Stock Units

The 2015 Plan also authorizes our compensation committee to grant stock units. Stock units represent the participant's right to receive a compensation amount, based on the value of the shares of common stock, if vesting criteria established by the compensation committee are met. If the vesting criteria are met, we will pay stock units in cash, shares of common stock or a combination of the two.

Annual Incentive Awards

Under the 2015 Plan, we may provide for performance-based bonuses payable in cash upon the attainment of performance goals that the compensation committee establishes related to one or more performance criteria described in the 2015 Plan over a performance period of up to one year. Like other performance-based awards, cash performance bonuses, for which there is no minimum payout, must be based upon objectively determinable bonus formulas established in accordance with the 2015 Plan, as determined by our compensation committee.

Dividend Equivalent Rights

Our compensation committee may grant dividend equivalent rights in connection with the grant of any equity-based award other than options and appreciation rights. Dividend equivalent rights may be paid currently or may be deemed to be reinvested in additional shares of stock, which may thereafter accrue additional dividend equivalent rights, and may be payable in cash, shares of common stock or a combination of the two. Our compensation committee will determine the terms of any dividend equivalent rights.

Performance Awards

The 2015 Plan will permit the grant of performance-based stock and cash awards that may qualify as performance-based compensation not subject to the $1,000,000 limitation on the income tax deductibility of compensation paid to a covered employee imposed by Section 162(m) of the Code. Under the 2015 Plan, our compensation committee may structure such awards so that stock is issued or cash is paid pursuant to such award only upon achievement of the performance goals set by our compensation committee at the beginning of the designated performance period which may be up to 10 years.

We may select performance goals based on one or more of the following measures: (1) net earnings or net income; (2) operating earnings; (3) pretax earnings; (4) earnings per share of stock; (5) stock price, including growth measures and total stockholder return; (6) earnings before interest and taxes; (7) earnings before interest, taxes, depreciation and/or amortization; (8) earnings before interest, taxes, depreciation and/or amortization as adjusted to exclude any one or more of the following: (i) stock-based compensation expense; (ii) income from discontinued operations; (iii) gain on cancellation of debt; (iv) debt extinguishment and related costs; (v) restructuring, separation, and/or integration charges and costs; (vi) reorganization and/or recapitalization charges and costs; (vii) impairment charges; (viii) merger-related events; (ix) gain or loss related to investments; (x) sales and use tax settlements; and (xi) gain on non-monetary transactions; (9) sales or revenue growth, whether in general, by type of product or service, or by type of customer; (10) gross or operating margins; (11) return measures, including return on assets, capital, investment, equity, sales or revenue; (12) cash flow, including operating cash flow, free cash flow, cash flow return on equity and cash flow return on investment; (13) productivity ratios; (14) expense targets; (15) market share; (16) financial ratios as provided in credit agreements of the company and its subsidiaries; (17) working capital targets; (18) completion of acquisitions of business or companies; (19) completion of divestitures and asset sales; (20) revenues under management; (21) funds from operations; (22) successful implementation of clinical trials, including components thereof; (23) submitting regulatory filings; (24) obtaining regulatory or marketing approvals; (25) entering into contractual agreements; (26) meeting contractual requirements; (27) achieving contractual milestones; (28) entering into collaborations; (29) receipt of grant funding; (30) developing or expanding manufacturing or production capacity; and (31) any combination of any of the foregoing business criteria.

We may base performance goals on a company-wide basis, with respect to one or more business units, divisions, affiliates or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. We may not adjust upward any awards that we intend to qualify as performance-based compensation under Section 162(m) of the Code. The plan administrator will retain the discretion to adjust performance-based awards downward, either on a formula or discretionary basis, or any combination as the compensation committee determines. Performance goals may differ from participant to participant and from award to award.

Other Equity-Based Awards

Our compensation committee may grant other types of equity-based awards under the 2015 Plan. Other equity-based awards may be payable in cash, shares of common stock or other equity, or a combination thereof, and may be restricted or unrestricted, as determined by our compensation committee. The terms and conditions that apply to other equity-based awards are determined by the compensation committee.

Change in Control

If we experience a change in control (as defined in the 2015 Plan) in which outstanding equity-based awards will not be assumed or continued by the surviving entity, unless otherwise provided in an award agreement, all restricted shares, stock units and dividend equivalent rights will vest, and the underlying shares will be delivered immediately before the change in control. In addition, all options and stock appreciation rights will become exercisable 15 days before the change in control and terminate upon the consummation of the change in control, and/or, in the discretion of our board of directors, all options, stock appreciation rights, restricted shares, stock units and dividend equivalent rights may be canceled before the change in control in exchange for payment of any amount in cash or securities having a value (as determined by our board of directors), in the case of restricted shares, stock units and dividend equivalent rights equal to the formula or fixed price per share paid to our stockholders and, in the case of options and stock appreciation rights equal to the product of the number of shares subject to the options or stock appreciation rights multiplied by the amount by which the formula or fixed price paid to our stockholders exceeds the exercise price of each option or the stock appreciation right. In the case of performance awards denominated in shares or units, if more than half of the performance period has lapsed, the awards will be converted into shares or units based upon actual performance achieved to date. If less than half of the performance period has lapsed, or if we cannot determine actual performance, the awards will be converted into shares or units assuming target performance has been achieved.

Amendment; Termination

Our board of directors may amend, suspend or terminate the 2015 Plan at any time; provided that no amendment, suspension or termination may adversely impair the rights of participants or obligations of ours under outstanding awards. Our stockholders must approve any amendment if such approval is required under applicable law or NASDAQ Listing Rules. Unless terminated sooner by our board of directors or extended with stockholder approval, the 2015 Plan will terminate on the 10th anniversary of the date of the completion of this offering.

2007 Stock Plan

General

In January 2007, our board of directors and our stockholders adopted the 2007 Plan. The 2007 Plan was most recently amended by our board of directors on August 18, 2015, which amendment was approved by our stockholders on August 20, 2015. Our board of directors administers the 2007 Plan. Our board of directors has determined not to grant any additional awards under the 2007 Plan after the completion of this offering. However, the 2007 Plan will continue to govern the terms and conditions of the outstanding awards granted under the 2007 Plan which, as of December 31, 2015, constitute stock options to purchase 2,606,195 shares of our common stock.

Share Reserve

As of December 31, 2015, a total of 3,003,374 shares of our common stock had been authorized for issuance under the 2007 Plan. As of December 31, 2015, options to purchase a total of 2,606,195 shares of our common stock were issued and outstanding, a total of 46,419 shares of our common stock had been issued upon the exercise of options or pursuant to other awards granted under the 2007 Plan, and 350,760 shares remained available for future grant. Such remaining share balance will become available for issuance under the 2015 Plan upon completion of this offering.

Types of Awards

The 2007 Plan provides for the grant of incentive stock options, non-statutory stock options and stock purchase rights to our employees, directors and consultants. Our 2007 Plan provides for the grant of incentive stock options, within the meaning of Section 422 of the Code, only to our employees or any of our "parent corporations" or "subsidiary corporations" (as such terms are defined in Sections 424(e) and (f) of the Code). Our board of directors has the authority to determine the terms and conditions of the awards granted under the 2007 Plan.

The 2007 Plan does not allow for the transfer of option awards or stock purchase rights other than by will or the laws of descent and distribution, and only the recipient of an award or a permitted transferee may exercise such award during his or her lifetime. Our board of directors, however, may in its discretion grant non-statutory stock options that may be transferred by instrument to an inter vivos or testamentary trust, or by gift or to an immediate family member.

Corporate Transaction

The 2007 Plan provides that in the event of our merger with or into another corporation, or a sale of all or substantially all of our assets, the successor corporation or its parent or subsidiary may assume or substitute for each outstanding award. If the outstanding awards are not assumed or substituted, such awards will terminate upon the consummation of the transaction.

2015 Employee Stock Purchase Plan

Our board of directors adopted the ESPP in September 2015, and our stockholders approved the ESPP in February 2016. The ESPP will become effective upon completion of this offering. The purpose of the ESPP is to enable our eligible employees, through payroll deductions or cash contributions, to purchase shares of our common stock, to increase our employees' interest in our growth and success and encourage employees to remain in our employment.

We reserved 250,000 shares of common stock for purchase by our eligible employees. In addition, effective January 1, 2017 and continuing until the expiration of the ESPP, the number of shares of common stock available for purchase by our eligible employees under the ESPP will automatically increase annually on January 1, in an amount equal to the lesser of (i) 1% of the total number of issued and outstanding shares of our common stock as of December 31 of the immediately preceding year, or (ii) 250,000 shares of our common stock, except that our board of directors may act prior to January 1 of any calendar year to provide for an increase of a lesser number of shares (which may be zero). In the event there is any change in the number of outstanding shares of our common stock, or the shares of common stock are changed into or exchanged for a different number or type of shares without receipt of consideration by us (for instance, by a recapitalization or stock split), we will proportionately adjust the number or type of shares that the eligible employees may purchase under the ESPP. The shares of common stock issuable under the ESPP may, in the discretion of our board of directors, be authorized but unissued shares, treasury shares or shares purchased on the open market. This summary is qualified in its entirety by the detailed provisions of the ESPP, which is filed as an exhibit to the registration statement of which this prospectus is a part.

Offering Periods and Optional Purchase Periods

Our compensation committee will determine the length and duration of the periods during which payroll deductions or other cash payments will accumulate to purchase shares of common stock, which period will not exceed 27 months. Each of these periods is known as an offering period.

Our compensation committee may, but is not required to, permit periodic purchases of common stock within a single offering period. The periods during which payroll deductions or other cash payments will accumulate for these purchases are referred to as purchase periods. We expect that each offering period will consist of a single purchase period for six months. No offering periods have been approved at this time.

Administration of the ESPP

Our compensation committee will administer the ESPP. Each member of our compensation committee that administers the ESPP will be both a “non-employee director” within the meaning of Rule 16b-3 of the Exchange Act and an “outside director” within the meaning of Section 162(m) of the Code. Our compensation committee will also interpret the provisions of the ESPP, prescribe, amend and rescind rules relating to it, and make all other determinations necessary or advisable in administering the ESPP, all of which determinations will be final and binding. During any period of time in which we do not have a compensation committee, another committee appointed by our board of directors will administer the ESPP. References to our compensation committee include a reference to any other committee appointed by our board of directors for those periods in which such other committee appointed by our board of directors is acting.

Eligibility

Any of our employees may participate in the ESPP, except: (i) an employee whose customary employment is less than 20 hours per week; and (ii) an employee who, after exercising his or her rights to purchase common stock under the ESPP, would own (directly or by attribution pursuant to Section 424(d) of the Code) shares of common stock (including shares that may be acquired under any outstanding options) representing 5% or more of the total combined voting power of all classes of our capital stock. An employee must be employed, as determined under the ESPP and applicable guidance, on the last trading day of the purchase period, or a purchase date, to acquire common stock under the ESPP, unless the employee has died prior to such time.

Participation Election

An eligible employee may participate in the ESPP by completing and submitting to us an enrollment form to participate. Such enrollment will authorize us to make payroll deductions on each pay day following enrollment in the ESPP, or if authorized by our compensation committee, participating employees may provide other cash contributions. Our compensation committee will credit the deductions or contributions to the employee's account under the ESPP. Subject to certain exceptions, an employee may not during any offering period change his or her percentage of payroll deduction or contribution for that offering period, nor may an employee withdraw any contributed funds. A participating employee may decrease his or her rate of contribution once during a purchase period (but not below $10 per pay period), or change his or her rate of contribution to take effect on the first day of the next offering period, by delivering to us a new enrollment form to participate in the ESPP. To the extent expressly permitted by our compensation committee, as determined in its sole discretion, for an offering period, a participating employee may increase the rate of his or her contribution once during the offering period. A participating employee may terminate payroll deductions or contributions at any time prior to a purchase date.

Purchase Price

Rights to purchase shares of our common stock will be deemed granted to participating employees as of the first trading day of each offering period. Our compensation committee will determine the purchase price for each share, or the purchase price. The purchase price for an offering period may not be less than 85% of the fair market value of our common stock on the first trading day of the offering period or the purchase date, whichever is lower, and in no event may the purchase price be less than the par value of our common stock.

Purchase Limit

No employee may purchase shares of our common stock in any offering period or in any calendar year under the ESPP and all other "employee stock purchase plans" of the company having an aggregate fair market value in excess of $25,000, determined as of the first trading date of the offering period. In addition, no employee may purchase more than 100,000 shares of common stock in any one offering period; provided that, prior to the start of an offering period, our compensation committee, in its discretion, may impose a different limit on the number or value of shares of common stock an employee may purchase during the offering period. We expect that participating employees will be able to contribute between 1% and 15% of their eligible earnings during an offering period.

Purchase of Common Stock

On each purchase date, a participating employee will be credited with the number of whole shares of common stock purchased under the ESPP during such purchase period. Shares of common stock purchased under the ESPP will be held in the custody of an agent designated by our board of directors. The agent may hold such shares in stock certificates by book entry or in nominee names and may commingle shares held in its custody in a single account or in stock certificates without identification as to individual participating employees. Subject to any additional restrictions imposed by our compensation committee, in its discretion, a participating employee may, at any time following his or her purchase of shares of common stock under the ESPP, instruct the agent to have all or part of such shares reissued in the employee's own name and have the stock certificate delivered to the employee. Our compensation committee may impose a holding period requirement of up to two years from the date participating employees purchase shares of common stock under the ESPP.

If in any purchase period the number of unsold shares that may be made available for purchase under the ESPP is insufficient to permit eligible employees to exercise their rights to purchase shares, our compensation committee will make a participation adjustment and proportionately reduce the number of shares purchasable by all participating employees. Our compensation committee will refund to a participating employee any funds then remaining in his or her account after such exercise.

Authorized Leave of Absence or Disability

Our compensation committee may suspend payroll deductions for a participating employee who remains an eligible employee during any period of absence of the employee from work due to an authorized leave of absence or disability or, if the employee so elects, he or she may continue to pay periodic cash contributions to the ESPP. If such participating employee returns to active service prior to a purchase date, the employee's payroll deductions will resume. If such employee did not make periodic cash contributions during the employee's period of absence, the employee may elect to either: (i) make up any deficiency in his or her account resulting from a suspension of payroll deductions by an immediate cash payment; (ii) not make up such deficiency in his or her account, in which event the number of shares to be purchased by the employee will be reduced to the number of whole shares that may be purchased with the amount, if any, credited to the employee's account on the purchase date, plus the aggregate amount, if any, of all payroll deductions to be made thereafter; or (iii) withdraw the amount in his or her account and terminate his or her option to purchase.

Termination of Participation

Our compensation committee will terminate a participating employee's participation in the ESPP and refund all monies in his or her account if: (i) our board of directors terminates the ESPP; or (ii) the employee ceases to be eligible to participate in the ESPP. In the event a participating employee's employment terminates, or is deemed terminated, for any reason other than death, the amount in the employee's account will be distributed and his or her option to purchase will terminate.

If a participating employee terminates participation in the ESPP on account of his or her death, the employee's representative may elect within three months after the employee's death to either: (a) purchase shares of common stock on the purchase date with the amount then credited to the employee's account; or (b) withdraw the amount in the employee's account. If the employee's representative fails to deliver notice of an election within the prescribed period, the election to participate will terminate and the amount in the employee's account will be paid to the employee's representative.

Transferability of Shares

No participating employee may transfer or assign his or her rights to purchase shares of common stock under the ESPP, whether voluntarily, by operation of law or otherwise. Any payment of cash or issuance of shares of common stock under the ESPP may be made only to the participating employee (or, in the event of the employee's death, to the employee's estate). During a participating employee's lifetime, only such participating employee may exercise his or her rights to purchase shares of common stock under the ESPP.

Amendment; Termination

Our board of directors may, at any time, amend the ESPP in any respect; provided that without stockholder approval, it may not (i) increase the number of shares that may be made available for

purchase under the ESPP, or (ii) change the eligibility requirements for participating in the ESPP. Additionally, our board of directors may not make any amendment to the ESPP that impairs the vested rights of participating employees. Our board of directors may suspend or terminate the ESPP at any time and for any reason or for no reason; provided that such suspension or termination will not impair any rights of participating employees that have vested at the time of termination. In any event, the ESPP will, without further action of our board of directors, terminate at the earlier of (a) 10 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.

Reorganizations

Upon our dissolution or liquidation, or upon a merger, consolidation or reorganization of the company with one or more other corporations in which we are not the surviving entity, or upon a sale of all or substantially all of our assets or any other transaction approved by our board of directors resulting in any person or entity owning more than 50% of the combined voting power of all classes of our capital stock, the ESPP and all rights outstanding thereunder will terminate, except to the extent provision is made in writing in connection with such transaction for the continuation or assumption of the ESPP, or for the substitution of the rights under the ESPP with new rights covering the stock of the successor entity. Upon termination of the ESPP in this circumstance, the offering period and the purchase period will end on the last trading day prior to such termination, and the rights of each participating employee shall be automatically exercised on such last trading day.

401(k) Retirement Plan

We maintain a defined contribution retirement plan for our employees. Our 401(k) plan is intended to qualify as a tax-qualified plan under Section 401 of the Code so that contributions to our 401(k) plan and income earned on such contributions are not taxable to participants until withdrawn or distributed from the 401(k) plan (except in the case of contributions under the 401(k) plan designated as Roth contributions, which are not taxable when distributed). Our 401(k) plan provides that each participant may contribute up to 100% of his or her pre-tax compensation, up to a statutory limit of $17,500 for 2014 and $18,000 for 2015. Participants who are at least 50 years old can also make “catch-up” contributions, which in 2014 and 2015 may be up to an additional $5,500 and $6,000, respectively, above the statutory limit. Under our 401(k) plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan’s trustee. Our 401(k) plan also permits us to make discretionary and matching contributions, subject to established limits and a vesting schedule. Beginning June 2015, we began making matching contributions equal to 50% of an employee’s contribution up to a maximum of $3,000 each year.

Non-Employee Director Compensation

Cash and Equity Compensation

In September 2015, our board of directors approved a non-employee director compensation policy, which will be effective for all non-employee directors upon the effective date of the registration statement for this offering. Each non-employee director will receive an annual base retainer of $35,000. In addition, our non-employee directors will receive the following cash compensation for board services, as applicable:

- the chairman of the board of directors will receive an additional annual retainer of $35,000;

- each member of our audit, compensation and nominating and corporate governance committees, other than the chairperson, will receive an additional annual retainer of $8,500, $6,500 and $4,000, respectively; and
- each chairperson of our audit, compensation and nominating and corporate governance committees will receive an additional annual retainer of $17,000, $13,000 and $8,000, respectively.

We will pay all amounts in quarterly installments. We will also reimburse each of our directors for their travel expenses incurred in connection with their attendance at board of directors and committee meetings.

Each non-employee director will also receive an annual award of options to purchase 8,000 shares of our common stock; provided, however, that if the closing of our initial public offering occurs (i) on or before March 31, 2016, non-employee directors will receive the annual award of options at our 2016 annual meeting of stockholders or (ii) after March 31, 2016, non-employee directors will receive the annual award of options upon the closing of our initial public offering, or the Annual Option Award. Each Annual Option Award will vest on the one-year anniversary of the date of grant, subject to the director's continued service on the board of directors.

Newly appointed non-employee directors will receive at the time of his or her appointment to the board of directors, a one-time initial award of options to purchase 20,000 shares of our common stock; provided, however, that if a director's appointment occurs within six months of our next annual meeting of stockholders, such director will be ineligible to receive their Annual Option Award in connection with such meeting. Each newly appointed non-employee director grant will vest monthly over a three-year period.

Director Compensation

Directors who are also our employees receive no additional compensation for their service as directors. The following table provides information regarding compensation awarded to or earned by our non-employee directors as of December 31, 2015.

Name	Fees Earned or Paid in Cash ($)	Option Award ($)[1][3]	All other compensation ($)	Total ($)
Dennis G. Podlesak	—	432,925	350,000[2]	782,925
Henry Chen	—	108,300	—	108,300
Fabrice Egros, Ph.D.	—	90,250	—	90,250
Luke Evnin, Ph.D.	—	126,349	—	126,349
Kim P. Kamdar, Ph.D.	—	108,300	—	108,300
Ivor Royston, M.D.	—	90,250	—	90,250
Richard P. Shea	52,000	126,349	—	178,349
George W. Sledge Jr., M.D.	63,000	126,349	—	189,349

(1) Amounts reflect the grant date fair value of option awards determined in accordance with ASC 718. For information regarding assumptions underlying the value of equity awards, see Note 12 to our audited consolidated financial statements and the discussion in the section titled "Management's Discussion and Analysis of Financial Condition and Results of Operations—Critical Accounting Policies—Stock-Based Compensation," included elsewhere in this prospectus. These amounts do not correspond to the actual value the director may realize upon exercise of these option awards.

(2) Amount reflects a one-time bonus granted to Mr. Podlesak for his efforts related to the Company's Series C-1 convertible preferred stock financing.
(3) The following table provides information regarding equity awards granted to our non-employee directors that were outstanding as of December 31, 2015.

Name	Option Awards Outstanding at Year-End
Dennis G. Podlesak	136,415
Henry Chen	14,400
Fabrice Egros, Ph.D.	22,167
Luke Evnin, Ph.D.	26,967
Kim P. Kamdar, Ph.D.	—
Ivor Royston, M.D.	22,167
Richard P. Shea	26,966
George W. Sledge Jr., M.D.	26,966

Limitation of Liability and Indemnification Agreements

Our amended and restated certificate of incorporation and amended and restated bylaws, each to become effective immediately prior to the completion of this offering, provide that we will limit the liability of our directors, and may indemnify our directors and officers, to the maximum extent permitted by the Delaware General Corporation Law, or DGCL. The DGCL provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except for liability for any:

- breach of their duty of loyalty to the corporation or its stockholders;
- act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or redemption of shares; or
- transaction from which the directors derived an improper personal benefit.

These limitations of liability do not apply to liabilities arising under federal securities laws and do not affect the availability of equitable remedies such as injunctive relief or rescission.

We entered into separate indemnification agreements with our directors and officers in addition to the indemnification provided for in our amended and restated bylaws. These indemnification agreements provide, among other things, that we will indemnify our directors and officers for certain expenses, including damages, judgments, fines, penalties, settlements and costs and attorneys' fees and disbursements, incurred by a director or officer in any claim, action or proceeding arising in his or her capacity as a director or officer of our company or in connection with service at our request for another corporation or entity. The indemnification agreements also provide for procedures that will apply in the event that a director or officer makes a claim for indemnification.

We also maintain a directors' and officers' insurance policy pursuant to which our directors and officers are insured against liability for actions taken in their capacities as directors and officers. We believe that these indemnification provisions and insurance are useful to attract and retain qualified directors and officers.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

The following is a description of transactions, since January 1, 2013, to which we have been a party or will be a party, in which the amount involved exceeded or will exceed $120,000, and in which any of our executive officers, directors or holders of more than 5% of any class of our voting securities, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest, other than compensation, termination and change of control arrangements, which are described under the section titled “Executive and Director Compensation.” We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that we would pay or receive, as applicable, in arm’s-length transactions with unrelated third parties.

Bridge Financings

December 2011 Bridge Financing

On December 20, 2011, we entered into a bridge loan financing, or the December 2011 bridge financing, in which we issued (i) convertible promissory notes, or the December 2011 notes, for (a) an aggregate principal amount of $2.5 million on December 20, 2011, (b) an aggregate principal amount of $0.4 million on December 28, 2011, (c) an aggregate principal amount of $2.9 million on April 2, 2012 and (d) an aggregate principal amount of $3.0 million on June 28, 2012, and (ii) warrants, or the December 2011 warrants, to purchase shares of our common stock at an exercise price of $38.44 per share, subject to adjustments upon the occurrence of certain events, at a purchase price of 0.1% of the principal amount of the December 2011 notes. The December 2011 notes accrued interest at a rate of 8% per annum and had a maturity date of December 31, 2012. On March 8, 2013, the December 2011 notes converted into 61,191 shares of our Series B convertible preferred stock and 608,312 shares of our Series B-1 convertible preferred stock, and the December 2011 warrants were canceled pursuant to the warrant cancellation agreement.

The following table summarizes the participation in the December 2011 bridge financing by holders of more than 5% of our capital stock and their affiliated entities:

Name	Aggregate Loan Amount ($)
Funds affiliated with Domain Associates	2,987,760[1]
Funds affiliated with MPM Capital	2,589,392[2]
Funds affiliated with Forward Ventures	717,062[3]

(1) Consists of (a) two notes held by Domain Partners VI, L.P., or Domain VI, each with a principal amount of $937,500 and (b) a note held by Domain VI with a principal amount of $1,112,760. Mr. Podlesak and Dr. Kamdar, members of our board of directors, are partners of Domain Associates, LLC, or Domain LLC, the manager of Domain VI.

(2) Consists of (a) two notes held by MPM BioVentures IV-QP, L.P., or MPM IV-QP, each with a principal amount of $676,896, (b) a note held by MPM IV-QP with a principal amount of $803,438, (c) two notes held by MPM BioVentures IV Strategic Fund, L.P., or MPM Strategic Fund, each with a principal amount of $90,278, (d) a note held by MPM Strategic Fund with a principal amount of $107,155, (e) two notes held by MPM BioVentures IV GMBH & Co. Beteiligungs KG, or MPM Beteiligungs, each with a principal amount of $26,078, (f) a note held by MPM Beteiligungs with a principal amount of $30,953, (g) two notes held by MPM Asset Management Investors BV4 LLC, or MPM BV4, each with a principal amount of $19,248 and (h) a note held by MPM BV4 with a principal amount of $22,846. Dr. Evnin, a member of our board of directors, is a member of MPM BioVentures IV LLC, or MPM IV LLC, which is the managing

member of MPM BioVentures IV GP LLC, or MPM IV GP, which is (i) the general partner of each of MPM IV-QP and MPM Strategic Fund, and (ii) the managing limited partner of MPM Beteiligungs. MPM IV LLC is the manager of MPM BV4.

(3) Consists of (a) two notes held by Forward Ventures V, LP, or Forward V, each with a principal amount of $150,000, (b) a note held by Forward V with a principal amount of $178,041, (c) two notes held by Forward Ventures IV, LP, or Forward IV, each with a principal amount of $69,139, (d) a note held by Forward IV with a principal amount of $82,064, (e) two notes held by Forward Ventures IVB, LP, or Forward IVB, each with a principal amount of $5,861 and (f) a note held by Forward IVB with a principal amount of $6,957. Dr. Royston, a member of our board of directors, is a managing member of Forward Ventures, a managing member of Forward IV Associates, LLC, or Forward IV Associates, and a member of Forward V. Forward IV Associates is the general partner of each of Forward IV and Forward IVB. Forward V Associates, L.L.C., or Forward V Associates, is the general partner of Forward V.

October 2012 Bridge Financing

On October 9, 2012, we entered into a bridge loan financing, or the October 2012 bridge financing, in which we issued convertible promissory notes, or the October 2012 notes, for an aggregate principal amount of $0.8 million. The October 2012 notes accrued interest at a rate of 8% per annum and had a maturity date of October 9, 2013. On March 8, 2013, the October 2012 notes converted into 5,536 shares of our Series B convertible preferred stock and 49,830 shares of our Series B-1 convertible preferred stock.

The following table summarizes the participation in the October 2012 bridge financing by holders of more than 5% of our capital stock and their affiliated entities:

Name	Aggregate Loan Amount ($)
Funds affiliated with Domain Associates	281,250(1)
Funds affiliated with MPM Capital	243,749(2)
Funds affiliated with Forward Ventures	67,500(3)

(1) Consists of a note held by Domain VI with a principal amount of $281,250. Mr. Podlesak and Dr. Kamdar, members of our board of directors, are partners of Domain LLC, the manager of Domain VI.

(2) Consists of (a) a note held by MPM IV-QP with a principal amount of $203,069, (b) a note held by MPM Strategic Fund with a principal amount of $27,083, (c) a note held by MPM Beteiligungs with a principal amount of $7,823 and (d) a note held by MPM BV4 with a principal amount of $5,774. Dr. Evnin, a member of our board of directors, is a member of MPM IV LLC, which is the managing member of MPM IV GP, which is (i) the general partner of each of MPM IV-QP and MPM Strategic Fund, and (ii) the managing limited partner of MPM Beteiligungs. MPM IV LLC is the manager of MPM BV4.

(3) Consists of (a) a note held by Forward V with a principal amount of $45,000, (b) a note held by Forward IV with a principal amount of $20,742 and (c) a note held by Forward IVB with a principal amount of $1,758. Dr. Royston, a member of our board of directors, is a managing member of Forward Ventures, a managing member of Forward IV Associates and a member of Forward V. Forward IV Associates is the general partner of each of Forward IV and Forward IVB. Forward V Associates is the general partner of Forward V.

November 2012 Bridge Financing

On November 19, 2012, we entered into a bridge loan financing, or the November 2012 bridge financing, in which we issued convertible promissory notes, or the November 2012 notes, for (i) an aggregate principal amount of $0.5 million on November 19, 2012, which had a maturity date of November 19, 2013, (ii) an aggregate principal amount of $0.5 million on November 30, 2012, which had a maturity date of November 30, 2013, (iii) an aggregate principal amount of $0.5 million on

December 28, 2012, which had a maturity date of December 28, 2013 and (iv) an aggregate principal amount of $0.7 million on January 18, 2013, which had a maturity date of January 18, 2014. The November 2012 notes accrued interest at a rate of 8% per annum. On March 8, 2013, the November 2012 notes converted into 157,045 shares of our Series B-1 convertible preferred stock.

The following table summarizes the participation in the November 2012 bridge financing by holders of more than 5% of our capital stock and their affiliated entities:

Name	Aggregate Loan Amount ($)
Funds affiliated with Domain Associates	1,026,000(1)
Funds affiliated with MPM Capital	701,998(2)
Funds affiliated with Forward Ventures	194,400(3)

(1) Consists of (a) two notes held by Domain Partners VIII, L.P., or Domain VIII, each with a principal amount of $235,751, (b) a note held by Domain VIII with a principal amount of $330,051, (c) a note held by Domain VIII with a principal amount of $216,891, (d) two notes held by DP VIII Associates, L.P., or DP VIII, each with a principal amount of $1,749, (e) a note held by DP VIII with a principal amount of $2,449 and (f) a note held by DP VIII with a principal amount of $1,609. Mr. Podlesak and Dr. Kamdar, members of our board of directors, are partners of Domain LLC, the manager of each of Domain VIII and DP VIII.

(2) Consists of (a) two notes held by MPM IV-QP, each with a principal amount of $135,380, (b) a note held by MPM IV-QP with a principal amount of $189,532, (c) a note held by MPM IV-QP with a principal amount of $124,550, (d) two notes held by MPM Strategic Fund, each with a principal amount of $18,055, (e) a note held by MPM Strategic Fund with a principal amount of $25,278, (f) a note held by MPM Strategic Fund with a principal amount of $16,611, (g) two notes held by MPM Beteiligungs, each with a principal amount of $5,215, (h) a note held by MPM Beteiligungs with a principal amount of $7,301, (i) a note held by MPM Beteiligungs with a principal amount of $4,798, (j) two notes held by MPM BV4, each with a principal amount of $3,849, (k) a note held by MPM BV4 with a principal amount of $5,389 and (l) a note held by MPM BV4 with a principal amount of $3,541. Dr. Evnin, a member of our board of directors, is a member of MPM IV LLC, which is the managing member of MPM IV GP, which is (i) the general partner of each of MPM IV-QP and MPM Strategic Fund, and (ii) the managing limited partner of MPM Beteiligungs. MPM IV LLC is the manager of MPM BV4.

(3) Consists of (a) two notes held by Forward V, each with a principal amount of $30,000, (b) a note held by Forward V with a principal amount of $42,000, (c) a note held by Forward V with a principal amount of $27,600, (d) two notes held by Forward IV, each with a principal amount of $13,828, (e) a note held by Forward IV with a principal amount of $19,359, (f) a note held by Forward IV with a principal amount of $12,722, (g) two notes held by Forward IVB, each with a principal amount of $1,172, (h) a note held by Forward IVB with a principal amount of $1,641 and (i) a note held by Forward IVB with a principal amount of $1,078. Dr. Royston, a member of our board of directors, is a managing member of Forward Ventures, a managing member of Forward IV Associates and a member of Forward V. Forward IV Associates is the general partner of each of Forward IV and Forward IVB. Forward V Associates is the general partner of Forward V.

September 2014 Bridge Financing

On September 18, 2014, we entered into a bridge loan financing, or the September 2014 bridge financing, in which we issued convertible unsecured promissory notes, or the September 2014 notes, for (i) an aggregate principal amount of $4,947,480 on September 18, 2014, which had a maturity date of September 30, 2015 and (ii) an aggregate principal amount of $52,520 on October 1, 2014, which had a maturity date of September 30, 2015. The September 2014 notes accrued interest at a rate of 6% per annum. On June 1, 2015, the September 2014 notes converted into 372,446 shares of our Series C-1 convertible preferred stock.

The following table summarizes the participation in the September 2014 bridge financing by holders of more than 5% of our capital stock and their affiliated entities:

Name	Aggregate Loan Amount ($)
Funds affiliated with Domain Associates	1,987,072(1)
Funds affiliated with MPM Capital	1,706,905(2)
Funds affiliated with Forward Ventures	472,682(3)
RMI Investments	780,821(4)

(1) Consists of (a) a note held by Domain VIII with a principal amount of $1,972,436 and (b) a note held by DP VIII with a principal amount of $14,636. Mr. Podlesak and Dr. Kamdar, members of our board of directors, are partners of Domain LLC, the manager of each of Domain VIII and DP VIII.

(2) Consists of (a) a note held by MPM IV-QP with a principal amount of $1,422,028, (b) a note held by MPM Strategic Fund with a principal amount of $189,656, (c) a note held by MPM Beteiligungs with a principal amount of $54,785 and (d) a note held by MPM BV4 with a principal amount of $40,436. Dr. Evnin, a member of our board of directors, is a member of MPM IV LLC, which is the managing member of MPM IV GP, which is (i) the general partner of each of MPM IV-QP and MPM Strategic Fund, and (ii) the managing limited partner of MPM Beteiligungs. MPM IV LLC is the manager of MPM BV4.

(3) Consists of (a) a note held by Forward V with a principal amount of $315,121, (b) a note held by Forward IV with a principal amount of $145,248 and (c) a note held by Forward IVB with a principal amount of $12,313. Dr. Royston, a member of our board of directors, is a managing member of Forward Ventures, a managing member of Forward IV Associates and a member of Forward V. Forward IV Associates is the general partner of each of Forward IV and Forward IVB. Forward V Associates is the general partner of Forward V.

(4) Consists of a note held by RMI Investments, S.á.r.l., or RMI, with a principal amount of $780,821.

Convertible Preferred Stock Financings

Conversion of Series A Convertible Preferred Stock

On March 8, 2013, in connection with the Series B-1 financing, 3,151,962 shares of our Series A convertible preferred stock converted into shares of our Series A-1 convertible preferred stock. The Series A convertible preferred stock was issued in 2007, 2008 and 2010 in exchange for convertible debt, accrued interest and cash, for gross cash proceeds of $49.0 million.

The following table sets forth the number of shares of Series A-1 convertible preferred stock received in the conversion of the Series A convertible preferred stock by holders of more than 5% of our capital stock and their affiliated entities. Each share of Series A-1 convertible preferred stock in the table below will convert into one share of our common stock upon completion of this offering.

Name	Series A Convertible Preferred Stock Converted (#)	Shares of Series A-1 Convertible Preferred Stock Issued Upon Conversion of Series A Convertible Preferred Stock (#)
Funds affiliated with Domain Associates(1)	1,313,319	1,313,319
Funds affiliated with MPM Capital(2)	1,138,210	1,138,210
Funds affiliated with Forward Ventures(3)	315,195	315,195

(1) Mr. Podlesak and Dr. Kamdar, members of our board of directors, are partners of Domain LLC.

(2) Dr. Evnin, a member of our board of directors, is a managing director of MPM Capital.

(3) Dr. Royston, a member of our board of directors, is a managing member of Forward Ventures.

Issuance of Series B-1 Convertible Preferred Stock

On March 8, 2013, we entered into the Series B-1 financing, pursuant to a Series B-1 preferred stock purchase agreement, or the Series B-1 purchase agreement, in which we agreed to sell up to 2,210,591 shares of our Series B-1 convertible preferred stock at a price per share of $14.00 in five tranches. The first tranche closed on March 8, 2013, at which time we issued 1,379,240 shares of Series B-1 convertible preferred stock, for net cash proceeds of $1.3 million and conversion of $18.7 million in principal amount of convertible notes and accrued interest thereon. In connection with the closing of the first tranche, the convertible notes we issued in the August 2010 bridge financing, December 2011 bridge financing, October 2012 bridge financing and November 2012 bridge financing and certain convertible notes we issued in February 2013 converted into either shares of Series B-1 convertible preferred stock or shares of Series B convertible preferred stock, contingent on whether the note holder invested its pro rata share in the Series B-1 financing. Collectively, these convertible notes converted into 1,284,550 shares of our Series B-1 convertible preferred stock and 118,522 shares of our Series B convertible preferred stock. The second tranche closed on April 30, 2013, at which time we issued 78,609 additional shares of Series B-1 convertible preferred stock, for gross cash proceeds of $1.1 million. In August 2013, we amended the Series B-1 purchase agreement in order to add RMI as a purchaser to the third tranche and any subsequent tranches. The third tranche closed on August 20, 2013, at which time we issued 484,219 additional shares of Series B-1 convertible preferred stock, for gross cash proceeds of $6.8 million. The Series B-1 purchase agreement provides for closings of fourth and fifth tranches upon the completion of certain closing conditions. In November 2013, we entered into an acknowledgement and waiver agreement with the purchasers of Series B-1 convertible preferred stock, pursuant to which the investors waived certain closing conditions relating to the date of closing of the fourth and fifth tranches, including the condition that we complete certain patent assignments as more fully described below. See the section titled “Certain Relationships and Related Party Transactions—NovaMedica Agreements.” Accordingly, the fourth and fifth tranches were accelerated and closed on November 20, 2013. At the closing of the fourth tranche, we issued 543,185 additional shares of Series B-1 convertible preferred stock, for gross cash proceeds of $7.6 million. At the closing of the fifth tranche, we issued 343,072 additional shares of Series B-1 convertible preferred stock, for gross cash proceeds of $4.8 million.

The tables below set forth the number of shares of Series B-1 convertible preferred stock purchased by holders of more than 5% of our capital stock and their affiliated entities in each of the five tranches of the Series B-1 financing. Each share of Series B-1 convertible preferred stock in the tables below will convert into one share of our common stock upon completion of this offering.

First Tranche—March 2013

Name	Series B-1 Convertible Preferred Stock (#)	Cancellation of Indebted-ness (Note Conversion) ($)	Cash Purchase Price of Series B-1 Convertible Preferred Stock ($)	Aggregate Purchase Price (including Note Conversion and Cash Purchase Price) ($)
Funds affiliated with Domain Associates[1]	560,216	7,283,713	554,472	7,838,185
Funds affiliated with MPM Capital[2]	471,324	6,118,207	476,294	6,594,501
Funds affiliated with Forward Ventures[3]	130,516	1,694,273	131,897	1,826,170

Second Tranche—April 2013

Name	Series B-1 Convertible Preferred Stock (#)	Aggregate Purchase Price of Series B-1 Convertible Preferred Stock ($)
Funds affiliated with Domain Associates(1)	32,898	460,316
Funds affiliated with MPM Capital(2)	28,258	395,414
Funds affiliated with Forward Ventures(3)	7,823	109,499

Third Tranche—August 2013

Name	Series B-1 Convertible Preferred Stock (#)	Aggregate Purchase Price of Series B-1 Convertible Preferred Stock ($)
Funds affiliated with Domain Associates(1)	113,495	1,587,973
Funds affiliated with MPM Capital(2)	97,491	1,364,076
Funds affiliated with Forward Ventures(3)	26,996	377,744
RMI Investments	243,008	3,400,000

Fourth Tranche—November 2013

Name	Series B-1 Convertible Preferred Stock (#)	Aggregate Purchase Price of Series B-1 Convertible Preferred Stock ($)
Funds affiliated with Domain Associates(1)	141,240	1,976,143
Funds affiliated with MPM Capital(2)	121,323	1,697,517
Funds affiliated with Forward Ventures(3)	33,596	470,082
RMI Investments	243,008	3,400,000

Fifth Tranche—November 2013

Name	Series B-1 Convertible Preferred Stock (#)	Aggregate Purchase Price of Series B-1 Convertible Preferred Stock ($)
RMI Investments	343,072	4,800,000

(1) Mr. Podlesak and Dr. Kamdar, members of our board of directors, are partners of Domain LLC.
(2) Dr. Evnin, a member of our board of directors, is a managing director of MPM Capital.
(3) Dr. Royston, a member of our board of directors, is a managing member of Forward Ventures.

Issuance of Series B-1 Convertible Preferred Stock

On April 18, 2013, we entered into a license and development agreement, or the Eddingpharm license agreement, with Eddingpharm International Company Limited, or Eddingpharm. In connection with the Eddingpharm license agreement, Eddingpharm agreed to purchase shares of our Series B-1 convertible preferred stock. On April 18, 2013, we entered into a preferred stock financing with Eddingpharm, or the Eddingpharm Series B-1 financing, in which we agreed to sell up to 357,365 shares of our Series B-1 convertible preferred stock at a price per share of $14.00 in two tranches. The first tranche closed on July 17, 2013, at which time we issued 178,682 shares of Series B-1 convertible preferred stock, for gross cash proceeds of $2.5 million. In November 2013, we entered into a letter agreement with Eddingpharm, pursuant to which Eddingpharm waived certain closing conditions

relating to the date of closing of the second tranche. Accordingly, the second tranche was accelerated and closed on November 15, 2013, at which time we issued 178,682 additional shares of Series B-1 convertible preferred stock, for gross cash proceeds of $2.5 million.

The tables below set forth the number of shares of Series B-1 convertible preferred stock purchased by Eddingpharm in each of the two tranches of the Eddingpharm Series B-1 financing. Each share of Series B-1 convertible preferred stock in the tables below will convert into one share of our common stock upon completion of this offering.

First Tranche—July 2013

Name	Series B-1 Convertible Preferred Stock (#)	Aggregate Purchase Price of Series B-1 Convertible Preferred Stock ($)
Eddingpharm	178,682	2,500,000

Second Tranche—November 2013

Name	Series B-1 Convertible Preferred Stock (#)	Aggregate Purchase Price of Series B-1 Convertible Preferred Stock ($)
Eddingpharm	178,682	2,500,000

In April 2015, Eddingpharm transferred all of the Series B-1 convertible preferred stock purchased by Eddingpharm in each of the two tranches of the Eddingpharm Series B-1 financing to its affiliate, Boom Profit Investments Limited.

Issuance of Series B-1 Convertible Preferred Stock

On December 19, 2014, we entered into a license, development and commercialization agreement, or the KHK license agreement, with Kyowa Hakko Kirin Co., Ltd, or KHK. In connection with the KHK license agreement, KHK agreed to purchase shares of our Series B-1 convertible preferred stock. On December 19, 2014, we entered into a preferred stock financing with KHK, or the KHK Series B-1 financing, in which we agreed to sell up to 536,049 shares of our Series B-1 convertible preferred stock at a price per share of $14.00. The KHK Series B-1 financing closed on January 6, 2015, at which time we issued 536,049 shares of Series B-1 convertible preferred stock, for gross cash proceeds of $7.5 million. Each share of Series B-1 convertible preferred stock issued in the KHK Series B-1 financing will convert into one share of our common stock upon completion of this offering.

Issuance of Series C-1 Convertible Preferred Stock

On June 1, 2015, we issued 1,340,113 shares of Series C-1 convertible preferred stock at a price per share of $14.00, pursuant to a Series C-1 preferred stock purchase agreement, or the June Series C-1 financing, for gross cash proceeds of $18.7 million. In connection with the June Series C-1 financing, the $5.0 million of convertible notes we issued in the September 2014 bridge financing and the related $0.2 million of accrued interest converted into 372,446 shares of Series C-1 convertible preferred stock.

The table below sets forth the number of shares of Series C-1 convertible preferred stock purchased by holders of more than 5% of our capital stock and their affiliated entities in the June Series C-1 financing. Each share of Series C-1 convertible preferred stock in the table below will convert into one share of our common stock upon completion of this offering.

Name	Series C-1 Convertible Preferred Stock (#)	Cancellation of Indebted-ness (Note Conversion) ($)	Cash Purchase Price of Series C-1 Convertible Preferred Stock ($)	Aggregate Purchase Price (including Note Conversion and Cash Purchase Price) ($)
Delos Investments 1[1]	804,073	—	11,249,995	11,249,995
Funds affiliated with Domain Associates[2]	363,314	2,071,019	3,012,238	5,083,257
Funds affiliated with MPM Capital[3]	312,085	1,779,016	2,587,519	4,366,535
Funds affiliated with Forward Ventures[4]	86,419	492,651	716,531	1,209,182
RMI Investments	142,764	813,808	1,183,660	1,997,468

(1) Mr. Chen, a member of our board of directors, is the managing partner of Delos Capital Fund, LP.
(2) Mr. Podlesak and Dr. Kamdar, members of our board of directors, are partners of Domain LLC.
(3) Dr. Evnin, a member of our board of directors, is a managing director of MPM Capital.
(4) Dr. Royston, a member of our board of directors, is a managing member of Forward Ventures.

Issuance of Series C-1 Convertible Preferred Stock

On August 21, 2015, we issued 4,377,902 shares of Series C-1 convertible preferred stock at a price per share of $14.00, pursuant to a Series C-1 preferred stock purchase agreement, or the August Series C-1 financing, for gross cash proceeds of $61.3 million.

The table below sets forth the number of shares of Series C-1 convertible preferred stock purchased by holders of more than 5% of our capital stock and their affiliated entities in the August Series C-1 financing. Each share of Series C-1 convertible preferred stock in the table below will convert into one share of our common stock upon completion of this offering.

Name	Series C-1 Convertible Preferred Stock (#)	Aggregate Purchase Price of Series C-1 Convertible Preferred Stock ($)
Delos Investments 1[1]	379,702	5,312,511
Funds affiliated with BlackRock, Inc.	714,730	9,999,994
Funds affiliated with Fidelity Management & Research Company	1,429,464	19,999,999

(1) Mr. Chen, a member of our board of directors, is the managing partner of Delos Capital Fund, LP.

NovaMedica Agreements

In connection with the third tranche of the Series B-1 financing in August 2013, we entered into a technology transfer agreement with Domain Russia Investments Limited, or DRI, an affiliate of Domain VIII. Domain VIII and Domain VI are both managed by Domain LLC. Pursuant to the technology transfer agreement, in exchange for a nominal payment, we assigned to DRI certain patent applications, or the assigned patents, in Armenia, Azerbaijan, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Ukraine and Uzbekistan, or the territory, and granted to DRI an exclusive, fully paid-up, royalty-free, irrevocable and assignable license under our other intellectual property to develop and commercialize entinostat and any other product containing the same active ingredient in the territory. We concurrently entered into a sublicense agreement, or the

DRI sublicense, with DRI and a sublicense agreement, or the NovaMedica sublicense, with NovaMedica LLC, or NovaMedica. NovaMedica is jointly owned by Rusnano Medinvest LLC, or Rusnano Medinvest, and DRI. RMI, a holder of more than 5% of our capital stock, is a wholly owned subsidiary of Rusnano Medinvest. Fabrice Egros, Ph.D., a member of our board of directors, was NovaMedica's Deputy Chief Executive Officer/Chief Operating Officer from November 2012 to September 2015 and a member of its board of directors from July 2012 to September 2015. Pursuant to the DRI sublicense, we granted to DRI an exclusive sublicense under the patents and other intellectual property licensed to us by Bayer to develop, manufacture and commercialize entinostat and any other product containing the same active ingredient in the Russian Federation. Pursuant to the NovaMedica sublicense, we granted to NovaMedica an exclusive sublicense under the patents and other intellectual property licensed to us by Bayer to develop, manufacture and commercialize entinostat and any other product containing the same active ingredient in the rest of the territory. Immediately thereafter, we, together with 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 technology transfer agreement and the DRI sublicense were transferred to NovaMedica. We agreed to perform all actions required to ensure that the patent assignments to DRI are registered and recorded in each country in the territory, and we agreed to provide all assistance that may be reasonably required to complete the subsequent transfer to NovaMedica of the assigned patents and DRI's rights under the technology transfer agreement and the DRI sublicense.

Under the terms of the technology transfer agreement, we have agreed, at NovaMedica's reasonable request, to facilitate NovaMedica's establishment of a manufacturing relationship with any of our third-party manufacturers. We also have agreed to provide NovaMedica with certain know-how and development and manufacturing support, including making our employees available to provide scientific and technical explanations, advice and support that may be reasonably required by NovaMedica. NovaMedica is required to reimburse us for any out-of-pocket expenses incurred by us in providing this assistance. In addition, we have agreed to sell to NovaMedica, at cost, our on-hand quantities of entinostat or any other product containing the same active ingredient to enable NovaMedica to conduct clinical trials of such product in the territory, so long as any sale does not reasonably interfere with our own development and commercialization activities.

In October 2013, we entered into a letter agreement with DRI pursuant to which we are obligated to indemnify DRI against certain third party claims. In particular, DRI, as an owner of NovaMedica, may be obligated under certain Russian loss compensation laws to make additional contributions to NovaMedica should the patent applications assigned by us to DRI under the technology transfer agreement, which were subsequently assigned by DRI to NovaMedica, diminish in value. We have agreed to indemnify DRI against any claims brought in respect of such Russian loss compensation laws, where such claims arise out of our breach of specified representations and warranties that we made in the technology transfer agreement, up to a maximum amount of $1.2 million.

At the same time that we entered into the technology transfer agreement, the DRI sublicense and the NovaMedica sublicense, we also entered into a clinical development and collaboration agreement, or the collaboration agreement, and a supply agreement with NovaMedica. The collaboration agreement establishes a framework under which we will consult with NovaMedica on development and regulatory issues relating to entinostat, including through various joint committees to be formed by the parties. Under the supply agreement, we are obligated to provide NovaMedica with a commercial supply of entinostat at a price to be negotiated in the future after the specifications for the commercial form of entinostat are finalized. Such price is limited to a fixed percentage mark-up over our costs. We

do not consider our agreements with DRI and NovaMedica to be material given the early stage of development of entinostat in the territory and immateriality of the market in the territory.

Investors' Rights Agreement

We are party to an amended and restated investors' rights agreement, or the investors' rights agreement, dated August 21, 2015, with the holders of our convertible preferred stock, certain holders of our common stock and Bayer. The investors' rights agreement provides that the holders of common stock issuable upon conversion of our convertible preferred stock have the right to demand that we file a registration statement or request that their shares of common stock be covered by a registration statement that we otherwise file. In addition to the registration rights, the investors' rights agreement provides for certain information rights and rights of first refusal. The provisions of the investors' rights agreement will terminate upon the completion of this offering, other than the registration rights which will terminate upon the earlier of (i) with respect to each stockholder, the date when such stockholder can sell all of its registrable shares in a single transaction pursuant to Rule 144 of the Securities Act, (ii) three years after this offering or (iii) a liquidating transaction as defined in our amended and restated certificate of incorporation, as currently in effect. The registration rights are described in more detail in the section titled "Description of Capital Stock—Registration Rights."

Voting Agreement

We have entered into an amended and restated voting agreement dated August 21, 2015, or the voting agreement, with certain holders of our common stock and certain holders of our convertible preferred stock. Pursuant to the voting agreement, holders of our Series A-1 convertible preferred stock, Series B-1 convertible preferred stock and Series C-1 convertible preferred stock have agreed to vote to approve the following: (i) one director to be a designee of Domain VIII, DP VIII, Domain VI and DP VI Associates, L.P., or DP VI, who is currently Kim P. Kamdar, Ph.D.; (ii) one director to be a designee of MPM IV-QP, who is currently Luke Evnin, Ph.D.; (iii) one director to be a designee of Forward V, Forward IV and Forward IVB, who is currently Ivor Royston, M.D.; (iv) one director to be a designee of RMI, who is Fabrice Egros, Ph.D.; and (v) one director to be a designee of Delos, who is currently Henry Chen. Certain holders of common stock have agreed to vote to approve the following: one director to be our Chief Executive Officer, who is currently Briggs W. Morrison, M.D.; and one director to be nominated by such holders of common stock, who is currently Dennis G. Podlesak. Certain holders of common stock and convertible preferred stock have agreed to vote together as a single class to nominate two directors who are not affiliates of us or any of our investors, to be designated as independent by unanimous approval of our board of directors, who are currently George W. Sledge Jr., M.D. and Richard P. Shea. The voting agreement will terminate upon the earlier of (i) the completion of this offering, (ii) a liquidating transaction as defined in the voting agreement or (iii) 10 years from the date of the voting agreement.

Other Transactions

We have entered into various employment related agreements and compensatory arrangements with our directors and executive officers that, among other things, provide for compensatory and certain severance and change of control benefits. For a description of these agreements and arrangements, see the section titled "Executive and Director Compensation—Executive Compensation—Employment Agreements."

We entered into separate indemnification agreements with our directors and officers. See the section titled “Executive and Director Compensation—Limitation of Liability and Indemnification Agreements.”

Policies and Procedures Regarding Transactions with Related Parties

In September 2015, our board of directors adopted a written related party transaction policy that will be in effect upon completion of this offering. Accordingly, following this offering, all proposed related party transactions must be approved by either (i) our nominating and corporate governance committee or (ii) our full board of directors. This review will cover any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships, in which we were or are to be a participant, the amount involved exceeds $120,000, and a related party had or will have a direct or indirect material interest, including purchases of goods or services by or from a related party in which the related party has a material interest, and indebtedness, guarantees of indebtedness and employment by us of a related party. A “related party” is any person who is or was one of our executive officers, directors or director nominees or is a holder of more than 5% of our common stock, or their immediate family members or any entity owned or controlled by any of the foregoing persons.

All of the transactions described above were entered into prior to the adoption of this policy and were approved by our board of directors.

PRINCIPAL STOCKHOLDERS

The following table sets forth certain information known to us regarding the beneficial ownership of our common stock as of February 15, 2016, and as adjusted to reflect the sale of shares of common stock in this offering and the conversion of all outstanding shares of our convertible preferred stock by:

- each of our named executive officers;
- each of our directors;
- all of our executive officers and directors as a group; and
- each person, or group of affiliated persons, known by us to beneficially own more than 5% of any class of our voting securities.

We have based our calculation of beneficial ownership prior to this offering on 12,972,675 shares of common stock outstanding on February 15, 2016, assuming the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 12,872,551 shares of our common stock upon completion of this offering. We have based our calculation of beneficial ownership after this offering on 17,372,675 shares of our common stock outstanding immediately following the completion of this offering, which gives effect to (i) the issuance of 4,400,000 shares of common stock in this offering and (ii) the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 12,872,551 shares of our common stock upon completion of this offering. Ownership information assumes no exercise of the underwriters' over-allotment option.

Information with respect to beneficial ownership has been furnished to us by each director, executive officer or stockholder who holds more than 5% of any class of our voting securities, as the case may be. Beneficial ownership is determined according to the rules of the SEC and generally means that a person has beneficial ownership of a security if he or she possesses sole or shared voting or investment power of that security, and includes options and warrants that are currently exercisable within 60 days of February 15, 2016. Options to purchase shares of our common stock that are exercisable within 60 days of February 15, 2016 are deemed to be beneficially owned by the persons holding these options for the purpose of computing percentage ownership of that person, but are not treated as outstanding for the purpose of computing any other person's ownership percentage. Except as indicated in the footnotes below, each of the beneficial owners named in the table below has, and upon completion of this offering will have, to our knowledge, sole voting and investment power with respect to all shares of common stock listed as beneficially owned by him or her, except for shares owned jointly with that person's spouse. Unless otherwise indicated, the address for each of the stockholders in the table below is c/o Syndax Pharmaceuticals, Inc., 400 Totten Pond Road, Suite 110, Waltham, Massachusetts 02451.

	Shares of Common Stock Beneficially Owned		Percentage of Shares Beneficially Owned	
Name and Address of Beneficial Owner	Before Offering	After Offering	Before Offering	After Offering
Named Executive Officers and Directors:				
Michael A. Metzger(1)	486,240	486,240	3.6%	2.7%
Michael L. Meyers(2)	162,079	162,079	1.2%	*
Arlene M. Morris(3)	308,553	308,553	2.3%	1.7%
Dennis G. Podlesak(4)	136,415	136,415	1.0%	*
Henry Chen(5)	14,400	14,400	*	*
Fabrice Egros, Ph.D. (6).	22,167	22,167	*	*
Luke Evnin, Ph.D.(7)	2,195,658	2,195,658	16.9%	12.6%
Kim P. Kamdar, Ph.D.(8)	25,847	25,847	*	*
Briggs W. Morrison, M.D.(9)	810,401	810,401	5.9%	4.5%
Ivor Royston, M.D.(10)	622,712	772,712	4.8%	4.4%
Richard P. Shea(11)	26,966	26,966	*	*
George W. Sledge Jr., M.D.(12)	26,966	26,966	*	*
All executive officers and directors as a group (14 persons)	5,125,051	5,275,051	33.5%	26.8%
5% Stockholders:				
Entities affiliated with BlackRock, Inc.(13)	714,730	1,264,730	5.5%	7.3%
Entities affiliated with Domain Associates(14)	2,538,046	2,538,046	19.6%	14.6%
Entities affiliated with FMR LLC(15)	1,456,106	2,121,106	11.2%	12.2%
Entities affiliated with MPM Capital(16)	2,168,691	2,168,691	16.7%	12.5%
Delos Investments 1(17)	1,183,775	1,183,775	9.1%	6.8%
RMI Investments(18)	971,852	971,852	7.5%	5.6%

* Represents beneficial ownership of less than 1% of our outstanding common stock.

(1) Consists solely of 486,240 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.

(2) Consists solely of 162,079 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.

(3) Consists solely of 308,553 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.

(4) Consists solely of 136,415 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016. Mr. Podlesak is a partner of Domain LLC. Mr. Podlesak has no voting or dispositive control over and disclaims beneficial ownership of the shares held by the entities affiliated with Domain LLC listed in footnote 14 below.

(5) Consists solely of 14,400 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.
(6) Consists solely of 22,167 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.
(7) Consists of (a) 26,967 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016, (b) 1,806,759 shares of common stock held by MPM IV-QP, (c) 240,963 shares of common stock held by MPM Strategic Fund, (d) 69,600 shares of common stock held by MPM Beteiligungs, and (e) 51,369 shares of common stock held by MPM BV4. Dr. Evnin is a member of MPM IV LLC, which is the managing member of MPM IV GP, which is (i) the general partner of each of MPM IV-QP and MPM Strategic Fund, and (ii) the managing limited partner of MPM Beteiligungs. MPM IV LLC is the manager of MPM BV4. Dr. Evnin shares power to vote, acquire, hold and dispose of the shares held by MPM IV-QP, MPM Strategic Fund, MPM Beteiligungs and MPM BV4, or collectively the MPM Entities. Dr. Evnin disclaims beneficial ownership of all shares held by the MPM Entities, except to the extent of his actual pecuniary interest therein.
(8) Consists of (a) 12,283 shares of common stock and (b) 13,564 shares of common stock held by Domain LLC. Dr. Kamdar is a managing member of Domain LLC, and shares voting and investment power over the shares held by Domain LLC. Dr. Kamdar disclaims beneficial ownership of all shares held by Domain LLC, except to the extent of her actual pecuniary interest therein.
(9) Consists solely of 810,401 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.
(10) Consists of (a) 22,167 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016, (b) 400,371 shares of common stock held by Forward V, (c) 184,539 shares of common stock held by Forward IV, and (d) 15,635 shares of common stock held by Forward IVB. In addition, the number of shares beneficially owned after this offering includes 150,000 shares of common stock purchased in this offering by entities affiliated with Forward V, Forward IV and Forward IVB. Dr. Royston is a member of Forward V and a managing member of Forward IV Associates, which is the general partner of each of Forward IV and Forward IVB. Forward V, Forward IV and Forward IVB are referred to herein as the Forward Entities. Dr. Royston shares voting and investment power over the shares held by the Forward Entities, and disclaims beneficial ownership of all shares held by the Forward Entities, except to the extent of his actual pecuniary interest therein.
(11) Consists solely of 26,966 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.
(12) Consists solely of 26,966 shares of common stock issuable upon the exercise of stock options within 60 days of February 15, 2016.
(13) Consists of (a) 668,208 shares of common stock held by BlackRock Health Sciences Opportunities Portfolio, a series of BlackRock Funds, (b) 35,428 shares of common stock held by BlackRock Health Sciences Trust and (c) 11,094 shares of common stock held by BlackRock Health Sciences Master Unit Trust. In addition, the number of shares beneficially owned after this offering includes 550,000 shares of common stock purchased in this offering by entities affiliated with BlackRock Health Sciences Opportunities Portfolio, a series of BlackRock Funds, BlackRock Health Sciences Trust and BlackRock Health Sciences Master Unit Trust. The registered holders of the referenced shares are funds and accounts under management by investment adviser subsidiaries of BlackRock, Inc. BlackRock, Inc. is the ultimate parent holding company of such investment adviser entities. On behalf of such investment adviser entities, Thomas Callan, as a managing director of such entities, has voting and investment power over the shares held by the funds and accounts which are the registered holders of the referenced shares. Thomas Callan expressly disclaims beneficial ownership of all shares held by such funds and accounts. The address of such funds and accounts, such investment adviser subsidiaries and Thomas Callan is 2929 Arch Street, 16th Floor, Philadelphia, PA 19104.
(14) Consists of (a) 1,743,854 shares of common stock held by Domain VI, (b) 761,062 shares of common stock held by Domain VIII, (c) 13,925 shares of common stock held by DP VI, (d) 5,641 shares of common stock held by DP VIII, and (e) 13,564 shares of common stock held by Domain LLC. One Palmer Square VI is the

general partner of each of Domain VI and DP VI, and One Palmer Square VIII is the general partner of each of Domain VIII and DP VIII. Domain VI, DP VI, Domain VIII, DP VIII and Domain LLC are referred to herein as the Domain Entities. James C. Blair, Brian H. Dovey, Jesse I. Treu, Kathleen K. Schoemaker and Nicole Vitullo, the managing members of One Palmer Square VI, share voting and investment power over the shares held by Domain VI and DP VI. James C. Blair, Brian H. Dovey, Jesse I. Treu, Kathleen K. Schoemaker, Brian K. Halak and Nicole Vitullo, the managing members of One Palmer Square VIII, share voting and investment power over the shares held by Domain VIII and DP VIII. James C. Blair, Brian H. Dovey, Jesse I. Treu, Kathleen K. Schoemaker, Brian K. Halak, Nicole Vitullo, Nimesh Shah and Dr. Kamdar, the managing members of Domain LLC, share voting and investment power over the shares held by Domain LLC. Each managing member of One Palmer Square VI, One Palmer Square VIII and Domain LLC disclaims beneficial ownership of all shares held by the Domain Entities, except to the extent of each such managing member's actual pecuniary interest therein. The address for the Domain Entities is One Palmer Square, Suite 515, Princeton, NJ 08542.

(15) Consists of (a) 1,153,417 shares of common stock held by Fidelity Select Portfolios: Biotechnology Portfolio, or Fidelity Select Portfolio, (b) 276,047 shares of common stock held by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, or Fidelity Advisors, and (c) 26,642 shares of common stock held by Fidelity Rutland Square Trust II: Strategic Advisers Small - Mid Cap Fund, or Fidelity Rutland. In addition, the number of shares beneficially owned after this offering includes 665,000 shares of common stock purchased in this offering by entities affiliated with Fidelity Select Portfolio, Fidelity Advisors and Fidelity Rutland. Fidelity Select Portfolio, Fidelity Advisors and Fidelity Rutland are managed by direct or indirect subsidiaries of FMR LLC. Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman and the President of FMR LLC. Members of the family of Edward C. Johnson 3d, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, or Fidelity Funds, advised by Fidelity Management & Research Company, or FMR Co, a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. Fidelity Management & Research Company carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address of entities affiliated with Fidelity Select Portfolio and Fidelity Advisors is 245 Summer Street, Boston, MA 02110.

(16) Consists of (a) 1,806,759 shares of common stock held by MPM IV-QP, (b) 240,963 shares of common stock held by MPM Strategic Fund, (c) 69,600 shares of common stock held by MPM Beteiligungs, and (d) 51,369 shares of common stock held by MPM BV4. MPM IV LLC is the managing member of MPM IV GP, which is (i) the general partner of each of MPM IV-QP and MPM Strategic Fund, and (ii) the managing limited partner of MPM Beteiligungs. MPM IV LLC is the manager of MPM BV4. Dr. Evnin, Ansbert Gadicke, Todd Foley, James Scopa and Vaughn Kailian, members of MPM IV LLC, share power to vote, acquire, hold and dispose of the shares held by the MPM Entities. Each member of MPM IV LLC disclaims beneficial ownership of all shares held by the MPM Entities, except to the extent of each such member's actual pecuniary interest therein. The address for the MPM Entities is 601 Gateway Blvd., Suite 350, South San Francisco, CA 94080.

(17) The address for Delos Investments 1 is 190 Elgin Avenue, George Town Grand Cayman KY1-9005, Cayman Islands.

(18) The address for RMI Investments is 7, Rue Robert Stümper, L-2557, Luxembourg.

DESCRIPTION OF CAPITAL STOCK

Immediately prior to the completion of this offering, our amended and restated certificate of incorporation will authorize us to issue up to 100,000,000 shares of common stock, par value $0.0001 per share and 10,000,000 shares of preferred stock, par value $0.001 per share. As of December 31, 2015, there were outstanding:

- 12,972,675 shares of our common stock held by approximately 59 stockholders (including 14,684 shares of unvested restricted stock subject to repurchase by us), which gives effect to the conversion of all outstanding shares of our convertible preferred stock into an aggregate of 12,872,551 shares of our common stock upon completion of this offering;
- 2,606,195 shares of our common stock subject to outstanding options; and
- 355,857 shares of our common stock issuable upon the exercise of the Bayer Warrant at an exercise price of $1.54 per share, based upon 19,978,870 shares of our common stock outstanding as of December 31, 2015 on a fully diluted basis immediately following this offering, which warrant is expected to remain outstanding upon completion of this offering.

The following description of our capital stock is not complete and is subject to and qualified in its entirety by our amended and restated certificate of incorporation and amended and restated bylaws and by the provisions of applicable Delaware law. Copies of these documents are filed with the SEC as exhibits to our registration statement, of which this prospectus forms a part. The descriptions of our common stock, preferred stock and warrant reflect changes to our capital structure that will occur immediately in connection with the completion of this offering.

Common Stock

Voting Rights

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders. The affirmative vote of holders of at least 66% of the voting power of all of the then-outstanding shares of capital stock, voting as a single class, will be required to amend certain provisions of our amended and restated certificate of incorporation, including provisions relating to amending our amended and restated bylaws, the classified board, the size of our board, removal of directors, director liability, vacancies on our board, special meetings, stockholder notices, actions by written consent and exclusive jurisdiction.

Dividends

Subject to preferences that may apply to any outstanding preferred stock, holders of our common stock are entitled to receive ratably any dividends that our board of directors may declare out of funds legally available for that purpose.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any outstanding preferred stock.

Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of our preferred stock that we may designate in the future.

Fully Paid and Nonassessable

All outstanding shares of our common stock are fully paid and non-assessable, and the shares of common stock to be issued upon completion of this offering will be fully paid and non-assessable.

Preferred Stock

Immediately prior to the completion of this offering, all outstanding shares of our preferred stock will convert into shares of common stock. Upon completion of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the number, rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences and sinking fund terms, and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action. We have no current plan to issue any shares of preferred stock.

Bayer Warrant

We issued the Bayer Warrant to Bayer to purchase such number of shares of our common stock initially equal to 1.75% of the shares of common stock outstanding on a fully diluted basis as of the earlier of the date of exercise or our initial public offering, at an exercise price of $1.54 per share. The Bayer Warrant contains a cashless exercise feature and Bayer may, at its option, exercise the Bayer Warrant in whole or in part at any time prior to expiration upon the earlier of (i) 10 years after our initial public offering or (ii) a consummation of a sale of all or substantially all of our assets or business.

Registration Rights

Holders of 13,259,554 shares of our convertible preferred stock, common stock, and common stock issuable upon exercise of the Bayer Warrant, have the right to demand that we file a registration statement or request that we cover their shares by a registration statement that we otherwise file, as described below.

Demand Registration Rights

At any time after 180 days after the completion of this offering, holders of at least 35% of the shares having demand registration rights may request that we register all or a portion of their shares of

common stock for sale under the Securities Act. We will effect the registration as requested, unless, in the good faith judgment of our board of directors, such registration would be seriously detrimental to the company and should be delayed. In addition, when we are eligible for the use of Form S-3, or any successor form, holders of at least 20% of the shares having demand registration rights may request that we register all or a portion of their common stock for sale under the Securities Act on Form S-3, or any successor form, so long as the aggregate price, net of underwriting discounts and commissions, to the public in connection with any such offering is more than $1.0 million.

Incidental Registration Rights

In addition, if at any time after this offering we register any shares of our common stock, the holders of all shares having piggyback registration rights are entitled to notice of the registration and to include all or a portion of their shares of common stock in the registration.

Other Provisions

In the event that any registration in which the holders of registrable shares participate pursuant to the investors' rights agreement is an underwritten public offering, the number of registrable shares to be included may, in specified circumstances, be limited due to market conditions.

We will pay all registration expenses, other than underwriting discounts, selling commissions and stock transfer taxes, and the reasonable fees and expenses of a single special counsel for the selling stockholders, related to any demand, piggyback and Form S-3 registration. The investors' rights agreement contains customary cross-indemnification provisions, pursuant to which we must indemnify the selling stockholders in the event of material misstatements or omissions in the registration statement attributable to us, and they must indemnify us for material misstatements or omissions in the registration statement attributable to them. The demand, piggyback and Form S-3 registration rights described above will expire, with respect to any particular stockholder, upon the earlier of (i) the date when such stockholder can sell all of its registrable shares in a single transaction pursuant to Rule 144 of the Securities Act, (ii) three years after our initial public offering or (iii) a liquidating transaction as defined in our amended and restated certificate of incorporation, as currently in effect.

Anti-Takeover Provisions

Certificate of Incorporation and Bylaws to be in Effect Immediately Prior to Completion of this Offering

Our amended and restated certificate of incorporation and amended and restated bylaws, each to become effective immediately prior to the completion of this offering, will include a number of provisions that may deter or impede hostile takeovers or changes of control or management. These provisions include:

- ***Issuance of Undesignated Preferred Stock***. After the filing of our amended and restated certificate of incorporation, our board of directors will have the authority, without further action by the stockholders, to issue up to 10,000,000 shares of undesignated preferred stock with rights and preferences, including voting rights, designated from time to time by our board of directors. The existence of authorized but unissued shares of preferred stock enables our board of directors to make it more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise.

- ***Classified Board***. Our amended and restated certificate of incorporation provides for a classified board of directors consisting of three classes of directors, with staggered three-year terms. Only one class of directors will be elected at each annual meeting of our stockholders, with the other classes continuing for the remainder of their respective three-year terms. This provision may have the effect of delaying a change in control of our board.
- ***Board of Directors Vacancies***. Our amended and restated certificate of incorporation and amended and restated bylaws authorize only our board of directors to fill vacant directorships. In addition, the number of directors constituting our board of directors may be set only by resolution adopted by a majority vote of our entire board of directors. These provisions prevent a stockholder from increasing the size of our board of directors and gaining control of our board of directors by filling the resulting vacancies with its own nominees.
- ***Stockholder Action; Special Meetings of Stockholders***. Our amended and restated certificate of incorporation provides that our stockholders may not take action by written consent, but may only take action at annual or special meetings of our stockholders. Stockholders will not be permitted to cumulate their votes for the election of directors. Our amended and restated certificate of incorporation further provides that only the chairman of our board of directors or a majority of our board of directors may call special meetings of our stockholders.
- ***Advance Notice Requirements for Stockholder Proposals and Director Nominations***. Our amended and restated bylaws provide advance notice procedures for stockholders seeking to bring business before our annual meeting of stockholders, or to nominate candidates for election as directors at our annual meeting of stockholders. Our amended and restated bylaws also specify certain requirements as to the form and content of a stockholder's notice. These provisions may make it more difficult for our stockholders to bring matters before our annual meeting of stockholders or to nominate directors at annual meetings of stockholders.

We designed these provisions to enhance the likelihood of continued stability in the composition of our board of directors and its policies, to discourage certain types of transactions that may involve an actual or threatened acquisition of us, and to reduce our vulnerability to an unsolicited acquisition proposal. We also designed these provisions to discourage certain tactics that may be used in proxy fights. However, these provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, they may also reduce fluctuations in the market price of our shares that could result from actual or rumored takeover attempts.

Section 203 of the Delaware General Corporation Law

We are subject to Section 203 of the DGCL, which prohibits a Delaware corporation from engaging in a business combination with any interested stockholder for a period of three years following the date the person became an interested stockholder, with the following exceptions:

- before such date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested holder;
- upon completion of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction began, excluding for purposes of determining the voting stock outstanding (but not the outstanding voting stock owned by the interested stockholder) those shares owned (a) by persons who are directors and also officers

and (b) pursuant to employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; and

- on or after such date, the business combination is approved by the board of directors and authorized at an annual or special meeting of the stockholders, and not by written consent, by the affirmative vote of at least 66 $^{2}/_{3}$% of the outstanding voting stock that is not owned by the interested stockholder.

In general, Section 203 of the DGCL defines business combination to include the following:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;
- subject to certain exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- any transaction involving the corporation that has the effect of increasing the proportionate share of the stock or any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits by or through the corporation.

In general, Section 203 of the DGCL defines an “interested stockholder” as an entity or person who, together with the entity’s or person’s affiliates and associates, beneficially owns, or is an affiliate of the corporation and within three years prior to the time of determination of interested stockholder status did own, 15% or more of the outstanding voting stock of the corporation.

A Delaware corporation may “opt out” of these provisions with an express provision in its certificate of incorporation. We have not opted out of these provisions, which may as a result, discourage or prevent mergers or other takeover or change of control attempts of us.

Choice of Forum

Our amended and restated certificate of incorporation will provide that unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall (or, if and only if the Court of Chancery of the State of Delaware lacks subject matter jurisdiction, any state court located within the State of Delaware or, if and only if all such state courts lack subject matter jurisdiction, the federal district court for the District of Delaware), the Court of Chancery of the State of Delaware will be the exclusive forum for (1) any derivative action or proceeding brought on our behalf, (2) any action or proceeding commenced by any of our stockholders (including any class action) asserting a breach of fiduciary duty owed, or other wrongdoing, by any director, officer, employee or agent to us or our stockholders, (3) any action or proceeding commenced by any of our stockholders (including any class action) asserting a claim against us arising pursuant to the DGCL or our amended and restated certificate of incorporation or our amended and restated bylaws, (4) any action or proceeding commenced by any of our stockholders (including any class action) to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws, or (5) any action or proceeding commenced by any of our stockholders (including any class action) asserting a claim against us that is governed by the internal affairs doctrine.

Transfer Agent and Registrar

Our transfer agent and registrar for our common stock is Computershare Trust Company, N.A.

The NASDAQ Global Select Market

Our common stock has been approved for listing on the NASDAQ Global Select Market under the trading symbol “SNDX.”

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, no public market for our common stock existed, and a liquid trading market for our common stock may not develop or be sustained after this offering. Future sales of substantial amounts of our common stock in the public market, including shares issued upon exercise of outstanding options and warrants, or the anticipation of such sales, could adversely affect prevailing market prices of our common stock from time to time and could impair our future ability to raise equity capital in the future. Furthermore, because only a limited number of shares of our common stock will be available for sale shortly after this offering due to certain contractual and legal restrictions on resale described below, sales of substantial amounts of our common stock in the public market after such restrictions lapse, or the anticipation of such sales, could adversely affect the prevailing market price of our common stock and our ability to raise equity capital in the future.

Based on the number of shares of common stock outstanding as of December 31, 2015 (including 14,684 shares of unvested restricted stock subject to repurchase by us), upon completion of this offering, 17,372,675 shares of our common stock will be outstanding. The number of shares outstanding upon completion of this offering assumes no exercise of outstanding options or the Bayer Warrant, and no exercise of the underwriters' over-allotment option.

All of the shares sold in this offering will be freely tradable unless purchased by our affiliates. The remaining 12,972,675 shares of common stock outstanding after this offering will be restricted as a result of securities laws or lock-up agreements as described below. Following the expiration of the lock-up period, all shares will be eligible for resale, subject to compliance with Rule 144 or Rule 701 of the Securities Act to the extent these shares have been released from any repurchase option that we may hold.

We may issue shares of common stock from time to time as consideration for future acquisitions, investments or other corporate purposes. In the event that any such acquisition, investment or other transaction is significant, the number of shares of common stock that we may issue may in turn be significant. We may also grant registration rights covering those shares of common stock issued in connection with any such acquisition and investment.

In addition, 4,962,052 shares of common stock that are either subject to outstanding options or warrants or reserved for future issuance under our equity incentive plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 of the Securities Act.

Rule 144

In general, under Rule 144 of the Securities Act, as in effect on the date of this prospectus, beginning 90 days after the date of this prospectus, any person who is not our affiliate at any time during the preceding three months, and who has beneficially owned their shares for at least six months, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares of our common stock provided current public information about us is available, and, after owning such shares for at least one year, including the holding period of any prior owner other than one of our affiliates, would be entitled to sell an unlimited number of shares of our common stock without restriction.

Beginning 90 days after the date of this prospectus, a person who is our affiliate or who was our affiliate at any time during the preceding three months, and who has beneficially owned restricted

securities for at least six months, including the holding period of any prior owner other than one of our affiliates, is entitled to sell within any three-month period a number of shares that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 173,727 shares, or 180,327 shares if the underwriters exercise their over-allotment option in full, immediately following this offering, based on the number of shares of our common stock outstanding upon completion of this offering; or
- the average weekly trading volume of our common stock on the NASDAQ Global Select Market during the four calendar weeks preceding the filing of a Notice of Proposed Sale of Securities pursuant to Rule 144 with respect to the sale.

Sales under Rule 144 by our affiliates are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

Upon expiration of the 180-day lock-up period described below, 12,972,675 shares of our common stock will be eligible for sale under Rule 144. We cannot estimate the number of shares of our common stock that our existing stockholders will elect to sell under Rule 144.

Rule 701

In general, under Rule 701 of the Securities Act, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act, is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

Lock-Up Agreements

We, along with our directors and executive officers and substantially all of our other stockholders have agreed with the underwriters that, for a period of 180 days following the date of this prospectus, we or they will not offer, sell, contract to sell, pledge, grant any option to purchase, make any short sale or otherwise dispose of any shares of our common stock (including any shares issued in this offering or other issuer-directed shares), or any options or warrants to purchase any shares of our common stock, or any securities convertible into, exchangeable for or that represent the right to receive shares of our common stock, whether now owned or later acquired, owned directly or with respect to which we or they have beneficial ownership within the rules and regulations of the SEC, subject to specified exceptions. The underwriters may, in their sole discretion, at any time without prior notice, release all or any portion of the shares from the restrictions in any such agreement.

Equity Incentive Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issuable under our equity incentive plans. We expect to file the registration statement covering such shares shortly after the date of this prospectus, permitting the resale of such shares by non-affiliates in the

public market without restriction under the Securities Act and the sale by affiliates in the public market, subject to compliance with the resale provisions of Rule 144. For more information on our equity incentive plans, see the section titled “Executive and Director Compensation—Equity Benefit Plans.”

Registration Rights

Holders of 13,259,554 shares of our convertible preferred stock, common stock, and common stock issuable upon exercise of the Bayer Warrant, have the right to demand that we file a registration statement or request that we cover their shares by a registration statement that we otherwise file. For more information, see the section titled “Description of Capital Stock—Registration Rights.” Except for shares purchased by affiliates, registration of their shares under the Securities Act would result in these shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration statement, subject to the expiration of the lock-up period and to the extent these shares have been released from any repurchase option that we may hold.

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following summary describes the material U.S. federal income tax consequences of the acquisition, ownership and disposition of our common stock acquired in this offering by Non-U.S. Holders (as defined below). This discussion does not address all aspects of U.S. federal income taxes and does not deal with foreign, state and local consequences that may be relevant to Non-U.S. Holders in light of their particular circumstances, nor does it address U.S. federal tax consequences other than income taxes and estate taxes to the limited extent set forth below. Special rules different from those described below may apply to certain Non-U.S. Holders that are subject to special treatment under the Code such as financial institutions, insurance companies, tax-exempt organizations, broker-dealers and traders in securities, U.S. expatriates, "controlled foreign corporations," "passive foreign investment companies," corporations that accumulate earnings to avoid U.S. federal income tax, persons that hold our common stock as part of a "straddle," "hedge," "conversion transaction," "synthetic security" or integrated investment or other risk reduction strategy, partnerships and other pass-through entities, and investors in such pass-through entities. Such Non-U.S. Holders are urged to consult their own tax advisors to determine the U.S. federal, state, local and other tax consequences that may be relevant to them. Furthermore, the discussion below is based upon the provisions of the Code, and Treasury regulations, rulings and judicial decisions thereunder as of the date hereof, and such authorities may be repealed, revoked or modified, perhaps retroactively, so as to result in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the U.S. Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS will agree with such statements and conclusions. This discussion assumes that the Non-U.S. Holder holds our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment).

The following discussion is for general information only and is not tax advice to any investor in light of their particular circumstances. Persons considering the purchase of our common stock pursuant to this offering should consult their own tax advisors concerning the U.S. federal income and estate tax consequences of acquiring, owning and disposing of our common stock in light of their particular situations as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local or foreign tax consequences.

For the purposes of this discussion, a "Non-U.S. Holder" is, for U.S. federal income tax purposes, a beneficial owner of common stock that is neither a U.S. Holder, a partnership (or other entity treated as a partnership for U.S. federal income tax purposes regardless of its place of organization or formation), nor an entity that is treated as a disregarded entity for U.S. federal income tax purposes (regardless of its place of organization or formation). A "U.S. Holder" means a beneficial owner of our common stock that is for U.S. federal income tax purposes (a) an individual who is a citizen or resident of the United States, (b) a corporation or other entity treated as a corporation created or organized in or under the laws of the United States, any state thereof or the District of Columbia, (c) an estate the income of which is subject to U.S. federal income taxation regardless of its source or (d) a trust if it (1) is subject to the primary supervision of a court within the United States and one or more U.S. persons have the authority to control all substantial decisions of the trust or (2) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person.

Distributions

Subject to the discussion below, distributions, if any, made on our common stock to a Non-U.S. Holder of our common stock to the extent made out of our current or accumulated earnings and profits

(as determined under U.S. federal income tax principles) generally will constitute dividends for U.S. tax purposes and will be subject to withholding tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. To obtain a reduced rate of withholding under a treaty, a Non-U.S. Holder generally will be required to provide us with a properly executed IRS Form W-8BEN or W-8BEN-E, or other appropriate form, certifying the Non-U.S. Holder's entitlement to benefits under that treaty. In the case of a Non-U.S. Holder that is an entity, Treasury regulations and the relevant tax treaty provide rules to determine whether, for purposes of determining the applicability of a tax treaty, dividends will be treated as paid to the entity or to those holding an interest in that entity. If a Non-U.S. Holder holds stock through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to such agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. If a Non-U.S. Holder is eligible for a reduced rate of U.S. federal withholding tax under an income tax treaty, the Non-U.S. Holder should contact its tax advisor regarding the possibility of obtaining a refund or credit of any excess amounts withheld by timely filing an appropriate claim for a refund with the IRS.

We generally are not required to withhold tax on dividends paid to a Non-U.S. Holder that are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, are attributable to a permanent establishment that such holder maintains in the United States) if a properly executed IRS Form W-8ECI, stating that the dividends are so connected, is furnished to us (or, if stock is held through a financial institution or other agent, to such agent). In general, such effectively connected dividends will be subject to U.S. federal income tax, on a net income basis at the regular graduated rates, unless a specific treaty exemption applies. A corporate Non-U.S. Holder receiving effectively connected dividends may also be subject to an additional "branch profits tax," which is imposed, under certain circumstances, at a rate of 30% (or such lower rate as may be specified by an applicable treaty) on the corporate Non-U.S. Holder's effectively connected earnings and profits, subject to certain adjustments.

To the extent distributions on our common stock, if any, exceed our current and accumulated earnings and profits, they will constitute a non-taxable return of capital and will first reduce the Non-U.S. Holder's adjusted basis in our common stock, but not below zero, and then will be treated as gain and taxed in the same manner as gain realized from a sale or other disposition of common stock as described in the next section.

For additional withholding rules that may apply to dividends paid to certain foreign entities, see the discussion below under the heading "Legislation Affecting Taxation of Our Common Stock Held by or Through Foreign Entities."

Gain on Disposition of Our Common Stock

Subject to the discussion below, a Non-U.S. Holder generally will not be subject to U.S. federal income tax with respect to gain realized on a sale or other disposition of our common stock unless (a) the gain is effectively connected with a trade or business of such holder in the United States (and, if required by an applicable income tax treaty, is attributable to a permanent establishment that such holder maintains in the United States), (b) the Non-U.S. Holder is a nonresident alien individual and is present in the United States for 183 or more days in the taxable year of the disposition and certain other conditions are met, or (c) we are or have been a "United States real property holding corporation" within the meaning of Code Section 897(c)(2) at any time within the shorter of the five-year period

preceding such disposition or such holder's holding period. In general, we would be a United States real property holding corporation if interests in U.S. real estate comprised (by fair market value) at least half of our business assets. We believe that we are not, and do not anticipate becoming, a United States real property holding corporation. Even if we are treated as a United States real property holding corporation, gain realized by a Non-U.S. Holder on a disposition of our common stock will not be subject to U.S. federal income tax so long as (1) the Non-U.S. Holder owned, directly, indirectly and constructively, no more than 5% of our common stock at all times within the shorter of (i) the five-year period preceding the disposition or (ii) the holder's holding period and (2) our common stock is regularly traded on an established securities market. There can be no assurance that our common stock will qualify as regularly traded on an established securities market.

If you are a Non-U.S. Holder described in (a) above, you will be required to pay tax on the net gain derived from the sale at regular graduated U.S. federal income tax rates, unless a specific treaty exemption applies, and corporate Non-U.S. Holders described in (a) above may be subject to the additional branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual Non-U.S. Holder described in (b) above, you will be required to pay a flat 30% tax on the gain derived from the sale, which gain may be offset by U.S. source capital losses (even though you are not considered a resident of the United States).

Information Reporting Requirements and Backup Withholding

Generally, we must report information to the IRS with respect to any dividends we pay on our common stock including the amount of any such dividends, the name and address of the recipient, and the amount, if any, of tax withheld. A similar report is sent to the holder to whom any such dividends are paid. Pursuant to tax treaties or certain other agreements, the IRS may make its reports available to tax authorities in the recipient's country of residence.

Dividends paid by us (or our paying agents) to a Non-U.S. Holder may also be subject to U.S. backup withholding. U.S. backup withholding generally will not apply to a Non-U.S. Holder who provides a properly executed IRS Form W-8BEN or W-8BEN-E or otherwise establishes an exemption. The current backup withholding rate is 28%.

Under current U.S. federal income tax law, U.S. information reporting and backup withholding requirements generally will apply to the proceeds of a disposition of our common stock effected by or through a U.S. office of any broker, U.S. or foreign, except that information reporting and such requirements may be avoided if the holder provides a properly executed IRS Form W-8BEN or W-8BEN-Eor otherwise meets documentary evidence requirements for establishing Non-U.S. Holder status or otherwise establishes an exemption. Generally, U.S. information reporting and backup withholding requirements will not apply to a payment of disposition proceeds to a Non-U.S. Holder where the transaction is effected outside the United States through a non-U.S. office of a non-U.S. broker. Information reporting and backup withholding requirements may, however, apply to a payment of disposition proceeds if the broker has actual knowledge, or reason to know, that the holder is, in fact, a U.S. person. For information reporting purposes, certain brokers with substantial U.S. ownership or operations will generally be treated in a manner similar to U.S. brokers.

Backup withholding is not an additional tax. A holder subject to backup withholding should contact the holder's tax advisor regarding the possibility of obtaining a refund or a tax credit and any associated requirements to provide information to the IRS or other relevant tax authority.

Legislation Affecting Taxation of Our Common Stock Held by or Through Foreign Entities

The Foreign Account Tax Compliance Act, or FATCA, which was enacted in 2010, imposes a 30% withholding tax on certain types of payments made to "foreign financial institutions" and certain other non-U.S. entities unless certain due diligence, reporting, withholding, and certification requirements are satisfied.

As a general matter, FATCA imposes a 30% withholding tax on dividends on, and gross proceeds from the sale or other disposition of, our common stock if paid to a foreign entity unless either (i) the foreign entity is a "foreign financial institution" that undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) the foreign entity is not a "foreign financial institution" and identifies certain of its U.S. investors, or (iii) the foreign entity otherwise is excepted under FATCA.

Pursuant to the delayed effective dates provided for in the final regulations, the required withholding with respect to dividends on our common stock began on July 1, 2014 and the required withholding with respect to gross proceeds from a sale or other disposition of our common stock will begin on January 1, 2017.

If withholding is required under FATCA on a payment related to our common stock, investors that otherwise would not be subject to withholding (or that otherwise would be entitled to a reduced rate of withholding) generally will be required to seek a refund or credit from the IRS to obtain the benefit of such exemption or reduction (provided that such benefit is available). Prospective investors should consult their tax advisors regarding the effect of FATCA in their particular circumstances.

Federal Estate Tax

An individual Non-U.S. Holder who is treated as the owner of, or has made certain lifetime transfers of, an interest in our common stock will be required to include the value thereof in his or her gross estate for U.S. federal estate tax purposes, and may be subject to U.S. federal estate tax unless an applicable estate tax treaty provides otherwise, even though such individual was not a citizen or resident of the United States at the time of his or her death.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE TO ANY INVESTOR IN LIGHT OF THEIR PARTICULAR CIRCUMSTANCES. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW.

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus, the underwriters named below, for whom Morgan Stanley & Co. LLC and Citigroup Global Markets Inc. are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Name	Number of Shares
Morgan Stanley & Co. LLC	1,760,000
Citigroup Global Markets Inc.	1,760,000
JMP Securities LLC	528,000
Oppenheimer & Co. Inc.	352,000
Total	4,400,000

The underwriters and the representatives are collectively referred to as the "underwriters" and the "representatives," respectively. The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the offering price listed on the cover page of this prospectus and part to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 660,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase about the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table.

The following table shows the per share and total public offering price, underwriting discounts and commissions, and proceeds before expenses to us. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase up to an additional 660,000 shares of common stock.

		Total	
	Per Share	No Exercise	Full Exercise
Public offering price	$ 12.00	$52,800,000	$60,720,000
Underwriting discounts and commissions to be paid by us:	$ 0.84	$ 3,696,000	$ 4,250,400
Proceeds, before expenses, to us	$ 11.16	$49,104,000	$56,469,600

The estimated offering expenses payable by us, exclusive of the underwriting discounts and commissions, are approximately $2,800,000. We have agreed to reimburse the underwriters for expenses relating to clearance of this offering with the Financial Industry Regulatory Authority, Inc. up to $25,000.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed 5% of the total number of shares of common stock offered by them.

Our common stock has been approved listed for listing on the NASDAQ Global Select Market under the trading symbol “SNDX.”

We and all directors and officers and the holders of substantially all of our outstanding stock, stock options and warrants have agreed that, without the prior written consent of Morgan Stanley & Co. LLC and Citigroup Global Markets Inc., on behalf of the underwriters, we and they will not, during the period until and including the 180th day after the date of this prospectus (the “restricted period”), directly or indirectly, offer, sell, pledge, contract to sell (including any short sale), grant any option to purchase or otherwise transfer or dispose of any shares of our common stock (including, without limitation, shares of common stock which may be deemed to be beneficially owned currently or hereafter in accordance with the rules and regulations of the SEC, shares of common stock which may be issued upon exercise of a stock option or warrant and any other security convertible into or exchangeable for common stock), enter into any short sale or any purchase, sale or grant of any right (including, without limitation, any put or call option) with respect to any security (other than a broad-based market basket or index) that includes, relates to or derives any significant part of its value from our common stock, or publicly announce any intention to do so.

The restrictions described in the immediately preceding paragraph to do not apply to us (i) to the extent that any such actions give effect to the transactions contemplated by the underwriting agreement for this offering, (ii) if we issue shares pursuant to the exercise of warrants outstanding as of the date of this prospectus and described in the registration statement and prospectus, but only if the holders of such shares or warrants agree in writing with the underwriters not to sell, offer, dispose of or otherwise transfer any such shares or warrants during the restricted period, (iii) if we issue shares or options to purchase shares, or issue shares upon exercise of options, pursuant to any stock option, stock bonus or other stock plan or arrangement described in the registration statement or prospectus, but only if the holders of such shares or options agree in writing with the underwriters not to sell, offer, dispose of or otherwise transfer any such shares or options during the restricted period and (iv) issue shares or any options or warrants or other rights to acquire shares or any securities exchangeable or exercisable for or convertible into shares (“Related Securities”), or to acquire other securities or rights ultimately exchangeable or exercisable for, or convertible into, shares in connection with a licensing arrangement, joint venture, acquisition or business combination or other collaboration or strategic transaction; *provided that*, in the case of clause (iv), recipients of such shares or Related Securities agree to be bound by the terms of the lock-up agreement and the sum of the aggregate number of shares or Related Securities so issued does not exceed 5% of the total outstanding shares of our common stock.

The restrictions described in the second preceding paragraph do not apply, in the case of our directors, officers and shareholders, to:

(a) the transfer of any or all of the shares of common stock or other securities if the transfer does not trigger any filing or reporting requirement or obligation or result in any other voluntary

or mandatory public disclosure under Section 16(a) of the Exchange Act, and the transfer is: (i) by gift, will or intestacy; (ii) to a trust whose beneficiaries consist exclusively such security holder or the family members of such security holder; (iii) a distribution to partners, members or shareholders of such security holder, or to any corporation, partnership or limited liability company that is an affiliate (within the meaning set forth in Rule 405 as promulgated by the SEC under the Securities Act) of such security holder; or (iv) to us upon the exercise of options to cover tax withholding obligations in connection with such exercise or for the primary purpose of paying the exercise price of options to acquire shares of common stock in each case pursuant to a stock option, stock bonus or other stock plan or arrangement existing as of the date of this prospectus and any shares acquired shall remain subject to the lock-up agreement; *provided*, that the transferee executes an agreement stating that the transferee is receiving and holding the securities subject to the provisions of the lock-up agreement;

(b) entering into any plan designed to satisfy the requirements of Rule 10b5-1 under the Exchange Act (other than the entry into such a plan in such a manner as to allow the sale of shares of common stock or other securities, in each case, within the restricted period); *provided however*, no public announcement or filing under the Exchange Act regarding the establishment of such 10b5-1 Plan shall be required or made during the restricted period; or

(c) (i) exercising any options, warrants or other rights to purchase shares of common stock pursuant to any stock option, stock bonus or other stock plan or any other arrangement existing as of the date of this prospectus (which exercises may be effected on a cashless basis to the extent the instruments representing such options, warrants or other rights permit exercises on a cashless basis) or (ii) the grant by us of stock options or other stock-based awards pursuant to any stock option, stock bonus or other stock plan or arrangement existing as of the date of this prospectus; *provided, however*, that in any such case, any shares of common stock or other securities acquired remain subject to the lock-up agreement, and *provided further*, that in the case of clause (i), such exercise does not trigger any filing or reporting requirement or obligation or result in any other voluntary or mandatory public disclosure under Section 16(a) of the Exchange Act during the restricted period.

Morgan Stanley & Co. LLC and Citigroup Global Markets Inc., in their sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of

common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of the common stock above independent market levels or prevent or retard a decline in the market price of the common stock. The underwriters are not required to engage in these activities and may end any of these activities at any time.

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

A prospectus in electronic format may be made available on websites maintained by one or more underwriters participating in this offering. The representatives may agree to allocate a number of shares of common stock to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters that may make Internet distributions on the same basis as other allocations.

Pricing of the Offering

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price were our future prospects and those of our industry in general, our current and prospective revenue and earnings, and certain other current and prospective financial and operating information, and the current and prospective price-earnings ratios, price-revenue ratios and market prices of securities, and certain current and prospective financial and operating information with respect to, companies engaged in activities similar to ours.

Other Relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. Certain of the underwriters and their respective affiliates have provided, and may in the future provide, a variety of these services to us and to persons and entities with relationships with us, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and their respective affiliates, officers, directors and employees may purchase, sell or hold a broad array of investments and actively trade securities, derivatives, loans, commodities, currencies, credit default swaps and other financial instruments for their own account and for the accounts of their customers, and such investment and trading activities may involve or relate to our assets, securities and instruments (directly, as collateral securing other obligations or otherwise) and/or persons and entities with relationships with us. The underwriters and their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such assets, securities or instruments and may at any time hold, or recommend to clients that they should acquire, long and/or short positions in such assets, securities and instruments.

Selling Restrictions

Canada

Shares of our common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of shares of our common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 (or, in the case of securities issued or guaranteed by the government of a non-Canadian jurisdiction, section 3A.4) of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State") an offer to the public of any shares of our common stock may not be made in that Relevant Member State, except that an offer to the public in that Relevant Member State of any shares of our common stock may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

(a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives for any such offer; or
(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares of our common stock in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares of our common stock to be offered so as to enable an investor to decide to purchase any shares of our common stock, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that

Member State, the expression “Prospectus Directive” means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State, and the expression “2010 PD Amending Directive” means Directive 2010/73/EU.

United Kingdom

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the FSMA) received by it in connection with the issue or sale of the shares of our common stock in circumstances in which Section 21(1) of the FSMA does not apply to us; and

(b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares of our common stock in, from or otherwise involving the United Kingdom.

LEGAL MATTERS

The validity of the shares of our common stock to be issued in this offering will be passed upon for us by our counsel, Hogan Lovells US LLP, Menlo Park, California. Certain legal matters relating to this offering will be passed upon for the underwriters by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements as of December 31, 2014 and 2015, and for the years then ended, included in this prospectus, have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein and elsewhere in the registration statement. Such consolidated financial statements have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of our common stock offered by this prospectus. This prospectus, which constitutes part of that registration statement, does not contain all of the information set forth in the registration statement or the accompanying exhibits and schedules. Some items included in the registration statement are omitted from this prospectus in accordance with the rules and regulations of the SEC. For further information with respect to us and the common stock offered in this prospectus, we refer you to the registration statement and the accompanying exhibits and schedules. Statements contained in this prospectus regarding the contents of any contract, agreement or any other document are summaries of the material terms of these contracts, agreements or other documents. With respect to each of these contracts, agreements or other documents filed as an exhibit to the registration statement, reference is made to such exhibit for a more complete description of the matter involved.

A copy of the registration statement and the accompanying exhibits and schedules and any other document we file may be inspected without charge and copied at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. The public may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The SEC maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the SEC's website is http://www.sec.gov.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act, and we will file periodic reports, proxy statements and other information with the SEC. These periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at http://www.syndax.com. You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports, proxy statements and other information filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The information contained in, or that can be accessed through, our website is not part of this prospectus.

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, 2014 and 2015, and the related consolidated statements of comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows for the years then ended. 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, 2014 and 2015, and the results of their operations and their cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

/s/ Deloitte & Touche LLP

Boston, Massachusetts
February 22, 2016 (February 24, 2016 as to the effects of the reverse stock split described in Note 17)

SYNDAX PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share data)

	December 31, 2014	December 31, 2015	Pro forma December 31, 2015 (unaudited)
ASSETS			
Current assets:			
Cash and cash equivalents	$ 10,009	$ 23,179	
Restricted cash	51	54	
Short-term investments	2,082	63,310	
Short-term deposits	117	805	
Prepaid expenses and other current assets	185	659	
Total current assets	12,444	88,007	
Property and equipment, net	33	88	
Other assets	339	1,808	
Total assets	$ 12,816	$ 89,903	
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' (DEFICIT) EQUITY			
Current liabilities:			
Current portion of long-term debt	$ 1,449	$ –	
Convertible notes	5,000	–	
Accounts payable	354	1,452	
Accrued expenses and other current liabilities	3,543	2,175	
Current portion of deferred revenue	–	1,220	
Total current liabilities	10,346	4,847	
Long-term liabilities:			
Long-term debt, less current portion	7,435	–	
Common stock warrant liability	693	2,848	$ –
Deferred revenue, less current portion	–	15,440	
Other long-term liabilities	58	70	
Total long-term liabilities	8,186	18,358	
Total liabilities	18,532	23,205	
Commitments (Note 14)			
Convertible preferred stock (Note 10)	146,853	319,113	–
Stockholders' (deficit) equity:			
Series A convertible preferred stock, $0.001 par value, 3,512,194 shares authorized at December 31, 2014 and 2015; 700,435 shares issued and outstanding at December 31, 2014 and 2015	7,231	7,231	–
Common stock, $0.0001 par value, 9,600,000 and 20,800,000 shares authorized at December 31, 2014 and 2015, respectively; 58,517 and 85,440 shares issued and outstanding at December 31, 2014 and 2015, respectively; 100,000,000 shares authorized; 12,957,991 shares issued and outstanding, pro forma (unaudited)	1	1	2
Additional paid-in capital	–	–	329,191
Accumulated other comprehensive income	–	28	28
Accumulated deficit	(159,801)	(259,675)	(259,675)
Total stockholders' (deficit) equity	(152,569)	(252,415)	$ 69,546
Total liabilities, convertible preferred stock and stockholders' (deficit) equity	$ 12,816	$ 89,903	

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

SYNDAX PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	Years Ended December 31,	
	2014	2015
Revenues:		
License fees	$ –	$ 627
Total revenues	–	627
Operating expenses:		
Research and development	10,175	9,549
General and administrative	11,157	11,591
Total operating expenses	21,332	21,140
Loss from operations	(21,332)	(20,513)
Other income (expense):		
Interest income	10	161
Interest expense	(299)	(1,575)
Change in fair value of common stock warrant liability	1,789	(2,155)
Other income (expense)	4	(37)
Total other income (expense)	1,504	(3,606)
Net loss	$(19,828)	$ (24,119)
Other comprehensive loss:		
Unrealized gains on marketable securities	$ –	$ 28
Comprehensive loss	$(19,828)	$ (24,091)
Net loss attributable to common stockholders	$(26,357)	$ (103,845)
Net loss per share attributable to common stockholders—basic and diluted	$(453.02)	$ (1,519.27)
Weighted-average common shares outstanding—basic and diluted	58,181	68,352
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		$ (2.28)
Pro forma weighted-average common shares used in net loss per share applicable to common stockholders—basic and diluted (unaudited)		9,597,519

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

SYNDAX PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' 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' 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)

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, 2014	2015
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (19,828)	$ (24,119)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	15	21
Amortization of debt discount and debt issuance costs	40	762
Amortization and accretion of investments	46	303
Stock-based compensation	2,257	3,882
Change in fair value of derivative	(4)	8
Change in fair value of warrants	(1,789)	2,155
Write-off of deferred costs associated with postponed IPO	4,319	–
Changes in operating assets and liabilities:		
Deposits	51	(718)
Prepaid expenses and other assets	13	(487)
Accounts payable	(726)	1,045
Deferred revenue	–	16,660
Accrued expenses and other liabilities	1,213	(1,940)
Net cash used in operating activities	(14,393)	(2,428)
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property and equipment	(4)	(49)
Increase in restricted cash	(1)	(118)
Purchases of short-term investments	(3,393)	(102,008)
Proceeds from sales and maturities of short-term investments	5,286	40,506
Net cash provided by (used in) investing activities	1,888	(61,669)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Principal payments on capital lease obligation	(2)	(2)
Proceeds from issuance of convertible preferred stock, net	–	87,323
Proceeds from issuance of debt	14,000	–
Proceeds from exercise of stock options	6	191
Deferred issuance costs	(1,594)	(1,245)
Payments on term loans	–	(9,000)
Net cash provided by financing activities	12,410	77,267
NET (DECREASE) INCREASE IN CASH AND CASH EQUIVALENTS	(95)	13,170
CASH AND CASH EQUIVALENTS—beginning of year	10,104	10,009
CASH AND CASH EQUIVALENTS—end of year	$ 10,009	$ 23,179
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:		
Interest paid	$ 170	$ 688
SUPPLEMENTAL DISCLOSURES OF NONCASH FINANCING ACTIVITIES:		
Accretion of convertible preferred stock to redemption value	$ –	$ 69,715
Accretion of dividends on convertible preferred stock	$ 6,529	$ 10,011
Conversion of convertible notes and accrued interest into Series C-1 convertible preferred stock	$ –	$ 5,211
Term loan proceeds allocated to derivative liability	$ 130	$ –
Deferred issuance costs included in accounts payable and accrued expenses	$ 614	$ 376
Property and equipment purchases included in accrued expenses	$ 3	$ 27
Vesting of restricted stock	$ –	$ 14

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

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Nature of Business and Summary of Significant Accounting Policies

Nature of Business – Syndax Pharmaceuticals, Inc. (the "Company") is a clinical stage biopharmaceutical company developing entinostat as a combination therapy in multiple cancer indications with an initial focus on tumors that have shown sensitivity to immunotherapy, including lung cancer, melanoma, ovarian cancer and triple negative breast cancer. The Company was incorporated under the laws of the State of Delaware on October 11, 2005 (date of inception) and is headquartered in Waltham, Massachusetts.

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"). The financial statements have been prepared on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the ordinary course of business. The financial statements do not include any adjustments relating to the recoverability and classification of recorded assets and liabilities that might be necessary should the Company be unable to continue as a going concern.

Management's Plans – 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 has financed its operations to date primarily with the proceeds from the sale of convertible preferred stock and the issuance of notes payable including the most recent preferred stock financing in August 2015, which resulted in net proceeds of $61.1 million, as described in Note 10.

The Company's long-term success is dependent upon its ability to successfully develop and market entinostat, 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 entinostat is approved and the Company begins to generate revenue from sales of entinostat; accordingly, management fully expects to incur substantial losses on the ongoing development of entinostat and does not expect to achieve positive cash flow from operations for the foreseeable future. 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 December 31, 2015 cash and short-term investments balances should enable the Company to maintain its current and essential 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 at 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.

Reverse Stock Split – On June 3, 2014, the Board of Directors (the "Board") and the stockholders of the Company approved a 1-for-12.3 reverse stock split of the Company's outstanding common stock and convertible preferred stock, which was effected on June 3, 2014. Stockholders entitled to fractional shares as a result of the

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

reverse stock split will receive 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 this reverse stock split.

Principles of Consolidation – 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.

Unaudited Pro Forma Information – The unaudited pro forma consolidated balance sheet information as of December 31, 2015, reflects (i) the conversion of 700,435 shares of Series A convertible preferred stock ("Series A") into 140,085 shares of common stock and (ii) the conversion of an aggregate of shares of Series A-1 convertible preferred stock ("Series A-1"), Series B convertible preferred stock ("Series B"), Series B-1 convertible preferred stock ("Series B-1") and Series C-1 convertible preferred stock ("Series C-1") into 12,732,466 shares of common stock, which along with the 85,440 shares of outstanding common stock will reflect an aggregate total of 12,957,991 shares of common stock immediately prior to the closing of the proposed initial public offering ("IPO"). Additionally, the common stock warrant liability has been reclassified to additional paid-in capital.

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, and U.S. government agency notes.

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 – Investments in 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' 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.

Revision of Interest Income and Interest Expense – The Company has revised its previous presentation of interest income and interest expense in the consolidated statements of comprehensive loss for the years ended December 31, 2014 and 2015 to correctly reflect $54,000 and $350,000 of amortization and accretion of the

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

Company's short-term investments in 2014 and 2015, respectively, as interest income rather than interest expense. This revision had no impact on total other income (expense) or net loss.

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 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 and issuance of debt. As of December 31, 2014 and 2015, the Company had capitalized deferred IPO issuance costs of $0 and $1.6 million, respectively. Future costs will be deferred until the completion of the IPO, at which time they will be reclassified to additional paid-in capital as a reduction of the IPO proceeds. If the Company terminates its plan for an IPO, any costs deferred will be expensed immediately. 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.

The deferred debt issuance costs are related to the Company's term loans and convertible notes and were amortized as interest expense over the period that the related debt was outstanding. For the years ended December 31, 2014 and 2015, amortization of debt issuance costs was $0 and $0.3 million, respectively, and as of December 31, 2014 and 2015, the Company had capitalized debt issuance costs of $0.3 million and $0, respectively.

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.

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 our product candidate, entinostat. 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.

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

Income Taxes – The Company records deferred tax assets and liabilities for the expected future tax consequences of temporary differences between the Company's financial statement carrying amounts and the tax bases of assets and liabilities and for loss and credit carryforwards using enacted tax rates expected to be in effect in the years in which the differences reverse. A valuation allowance is provided to reduce the net deferred tax

assets to the amount that will more likely than not be realized. The Company determines whether it is more likely than not that a tax position will be sustained upon examination. If it is not more likely than not that a position will be sustained, none of the benefit attributable to the position is recognized. The tax benefit to be recognized for any tax position that meets the more-likely-than-not recognition threshold is calculated as the largest amount that is more than 50% likely of being realized upon resolution of the contingency. The Company accounts for interest and penalties related to uncertain tax positions as part of its provision for income taxes.

Guarantees and Indemnifications – As permitted under Delaware law, the Company indemnifies its officers, directors, and employees for certain events or occurrences that happen by reason of the relationship with, or position held at, the Company. The Company has standard indemnification arrangements under office leases (as described in Note 14) that require it to indemnify the landlord against all costs, expenses, fines, suits, claims, demands, liabilities, and actions directly resulting from any breach, violation, or nonperformance of any covenant or condition of the Company's lease. Through December 31, 2015, 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 – The Company has classified certain series of convertible preferred stock as temporary equity in the consolidated balance sheets due to certain change in control events that are 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 is presented at its maximum redemption value. As of December 31, 2015, the Series A has no liquidation preference and is 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.

Derivative Liabilities – The Company records potential payments that would be made to lenders upon certain triggering events as a 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 recognized in other income (expense) in the consolidated statements of comprehensive loss 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 statements of comprehensive loss at each period end while such instruments are outstanding. The warrant liabilities were valued using a Black-Scholes option-pricing model.

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

Recently Issued Accounting Pronouncements – In May 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("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.

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. Early application is permitted. The Company is currently evaluating the impact of adopting ASU 2014-15 on its consolidated financial statements and related disclosures.

2. 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 years ended December 31, 2014 and 2015, 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,	
	2014	2015
Numerator—basic and diluted:		
Net loss	$ (19,828)	$ (24,119)
Accretion of convertible preferred stock dividends	(6,529)	(10,011)
Accretion of convertible preferred stock to redemption value	–	(69,715)
Net loss attributable to common stockholders—basic and diluted	$ (26,357)	$ (103,845)
Net loss per share—basic and diluted	$ (453.02)	$(1,519.27)
Denominator—basic and diluted:		
Weighted-average common shares used to compute net loss per share—basic and diluted	58,181	68,352

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

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,	
	2014	2015
Convertible preferred stock	6,246,041	12,872,551
Options to purchase common stock	831,148	2,606,195
Common stock warrants	127,099	277,486
Convertible notes and related accrued interest	363,294	–
Restricted stock subject to future vesting	–	14,684

The unaudited pro forma basic and diluted loss per share attributable to common stockholders for the year ended December 31, 2015 has been computed using the weighted-average number of shares of common stock outstanding after giving pro forma effect to (i) the automatic conversion of all shares of convertible preferred stock into shares of common stock and (ii) the conversion of convertible notes into shares of convertible preferred stock and then converted into shares of common stock as if such conversions had occurred at the beginning of the period presented or the date of original issuance, if later. Upon conversion of the convertible preferred stock into common stock in the event of an IPO, the holders on the convertible preferred stock are not entitled to receive undeclared dividends. Accordingly, the impact of the accretion of accrued but unpaid dividends has been excluded from the determination of net loss attributable to common stockholders as the holders of the convertible preferred stock are not entitled to receive accrued but unpaid dividends upon such conversion. The interest expense associated with the convertible debt has been excluded from the determination of net loss attributable to common stockholders as this expense would not have occurred if the notes had converted at the beginning of the period presented. The gains and losses associated with the changes in the fair value of the common stock warrant have been excluded from the determination of net loss attributable to common stockholders as these re-measurements would not have occurred if the common stock warrant converted at the beginning of the period presented.

Unaudited pro forma basic and diluted loss per share attributable to common stockholders are computed as follows (in thousands, except share and per share data):

	Year Ended December 31, 2015 (unaudited)
Numerator—basic and diluted:	
Net loss attributable to common stockholders—basic and diluted	$ (103,845)
Accretion of convertible preferred stock dividends	10,011
Accretion of convertible preferred stock to redemption value	69,715
Interest expense related to convertible notes	125
Change in fair value of common stock warrant liability	2,155
Pro forma net loss attributable to common stockholders—basic and diluted	$ (21,839)
Denominator—basic and diluted:	
Weighted-average number of shares outstanding—basic and diluted	68,352
Adjustment for assumed effect of conversion of convertible notes into common stock	155,109
Adjustment for assumed effect of conversion of convertible preferred stock	9,374,058
Pro forma weighted-average number of common shares used to compute pro forma net loss per share—basic and diluted	9,597,519
Pro forma net loss per share—basic and diluted	$ (2.28)

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

3. Significant Agreements

Merck KGaA – Pfizer Collaboration – On December 31, 2015, the Company entered into a clinical trial collaboration and supply agreement with Ares Trading, S.A., a subsidiary of Merck KGaA, Darmstadt, Germany, and Pfizer, Inc. (the "Alliance") under which it 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 the Alliance, which are together treated as a single party for purposes of this agreement. The Company will be the sponsor of the clinical trial. The Alliance will supply avelumab for use in the clinical trial. The Company will share the study costs equally with the Alliance. 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 prevents such party from supplying its drug, or if such party decides to discontinue development of its drug. The Alliance may also terminate the agreement if the Company fails to make any changes to the clinical trial protocol that are reasonably requested by the Alliance to address a perceived safety issue.

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.

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

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 will be 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 year ended December 31, 2015, the Company recognized $0.6 million of revenue associated with the KHK License Agreement. As of December 31, 2015, there was $16.7 million of deferred revenue related to the KHK License Agreement, which is classified as current or long-term in the consolidated balance sheets.

Eastern Cooperative Oncology Group – In March 2014, the Company entered into a clinical trial agreement (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. As of the effective date of the amendment to the ECOG Agreement, the Company's aggregate payment obligations under this agreement were approximately $20.6 million; and as of December 31, 2015, the Company's remaining payment obligations are approximately $18.3 million over an estimated period of approximately seven years.

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

The Company records the appropriate clinical trial expenses in its financial statements by matching those expenses with the period in which the services and efforts are expended. The Company accounts for these expenses according to the progress of the clinical trial as measured by patient enrollment and the timing of various aspects of the clinical trial. The Company determines accrual estimates through financial models, taking

into account discussion with applicable personnel and ECOG-ACRIN as to the progress or state of consummation of the clinical trial or the services completed.

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

In connection with the Bayer Agreement, the Company issued to Bayer a warrant to purchase the number of shares of the Company's common stock equal to 1.75% of the shares of common stock outstanding on a fully diluted basis as of the earlier of the date the warrant is exercised or the closing of the Company's IPO. The warrant contains 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 Company's IPO or the date of the consummation of a disposition transaction.

The warrant is classified as a long-term liability and recorded at fair value with the changes in the fair value recorded in other income (expense). The Company uses the Black-Scholes option-pricing model to determine the fair value of the warrant. 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 are as follows (in thousands, except share data):

December 31,	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
2014	127,099	$ 1.54	$ 6.27	72%	2.00%	0.0%	7.48	$ 693
2015	277,486	$ 1.54	$ 11.13	73%	2.15%	0.0%	8.06	$ 2,848

Upon the completion of the Company's IPO, the warrant will be reclassified to additional paid-in capital.

University of Colorado – In July 2007, the Company entered into an exclusive option agreement (the "Option Agreement") with the Regents of the University of Colorado ("Colorado"), whereby the Company was granted the exclusive 12-month option to license at a future date certain patents owned by Colorado. Under the terms of the Option Agreement, the Company agreed to reimburse Colorado for fees and costs incurred to date and ongoing patent prosecution costs. From September 2008 to December 2010, the Company paid Colorado a total of $0.1 million to extend the option period through December 31, 2010 for certain of the patents, and paid patent prosecution costs on those patents. In April 2013, the Company entered into an exclusive license agreement (the "Colorado Agreement") with Colorado for certain of the patents owned by Colorado. Under the terms of the Colorado Agreement, the Company will pay Colorado a license fee of $0.2 million, with $0.1 million payable within 30 days of execution of the Colorado Agreement and the balance upon the close of a

financing with proceeds specifically earmarked in writing for the development of a lung cancer indication involving the licensed patents. In each case, the license fee is payable in cash or the equivalent value of shares of the Company's common stock. Upon the execution of the Colorado Agreement in April 2013, the Company recorded a liability of $0.1 million in research and development expense. In November 2013, the Company issued 16,260 shares of its common stock to University License Equity Holdings, Inc. ("ULEH"), an affiliate of Colorado, to extinguish the liability and recorded additional research and development expense of $0.3 million to reflect the fair value of shares granted to ULEH. Under the Colorado Agreement, the Company is obligated to pay Colorado royalties on net sales, if any, and milestone payments related to the achievement of certain clinical and regulatory goals. As of December 31, 2014, none of these goals had been achieved; and no milestones were payable. The Colorado Agreement was terminated during the first quarter of 2015; and there were no incremental obligations in connection with the termination of the agreement.

4. Property and Equipment, net

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

	December 31,	
	2014	2015
Office and computer equipment	$ 131	$ 117
Furniture and fixtures	74	74
Office equipment under capital lease	13	13
Leasehold improvements	–	48
Construction in progress	–	28
Total property and equipment	218	280
Less: accumulated depreciation	(185)	(192)
Property and equipment, net	$ 33	$ 88

Property and equipment under capital leases consist of office equipment with a cost basis of $13,000 and accumulated amortization of $3,000 and $5,000, as of December 31, 2014 and 2015, respectively.

5. 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.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

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, 2014 and 2015.

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, 2014				
Assets:				
Cash equivalents	$ 4,986	$ 4,483	$ 503	$ –
Short-term investments	2,082	–	2,082	–
Total assets	$ 7,068	$ 4,483	$ 2,585	$ –
Liability:				
Derivative liability	$ 126	$ –	$ –	$ 126
Common stock warrant liability	$ 693	$ –	$ –	$ 693
Total liabilities	$ 819	$ –	$ –	$ 819
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 $4.5 million as of December 31, 2014 and $9.2 million as of December 31, 2015 consisted of money market funds and are classified within Level 1 of the fair value hierarchy because they are valued using quoted market prices in active markets. Cash equivalents of $0.5 million as of December 31, 2014 and $13.9 million as of December 31, 2015 consisted of 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.

Short-term investments of $2.1 million as of December 31, 2014 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.

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

The short-term investments are classified as available-for-sale securities; and as of December 31, 2015, the remaining contractual maturities of the available-for-sale securities were less than one year. At December 31, 2015, 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 12 months ended December 31, 2014 and 2015; and 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, 2015, 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, 2014				
Corporate bonds	$ 2,082	$ –	$ –	$ 2,082
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

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 warrants was considered a Level 3 measurement. See Note 3 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 was recorded at fair value using the following assumptions: weighted-average probability of 75% likelihood of a successful IPO in 0.08 years; 25% to the sale of the Company in 2.0 years; and a market-based discount rate that will increase or decrease each period based on changes in the probability in the future cash flows. A significant fluctuation in the probability would not result in a material increase or decrease in the fair value of the derivative liability.

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

6. Prepaid Expenses and Other Current Assets

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

	December 31,	
	2014	2015
Prepaid clinical supplies	$ –	$210
Interest receivable on short-term investments	35	258
Other	150	191
Total prepaid expenses and other current assets	$185	$659

7. Accrued Expenses and Other Current Liabilities

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

	December 31,	
	2014	2015
Accrued license fees	$1,000	$ 25
Accrued professional fees	954	561
Accrued compensation and related costs	653	698
Accrued clinical costs	646	574
Derivative liability	126	133
Accrued interest	124	–
Other	40	184
Total accrued expenses	$3,543	$2,175

8. 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.

9. 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.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

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.

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.

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; and 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.

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 has recorded the success fee as a derivative financial liability. The initial fair value of the derivative of $0.1 million has been recorded as a debt discount. The term loans were paid in full in October 2015; however, the liability for the success fee has survived the repayment of the term loans and will be due and payable upon the events described above.

10. Convertible Preferred Stock

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

December 31, 2014	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	$ 44,896	$ 62,530
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	3,031,971	$ 79,239	$ 79,239
Total					$146,853
Series A	3,512,194	March and August 2013	700,435	$ –	$ 7,231

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

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 accordance with the terms of the KHK License Agreement in January 2015, 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.

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 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.

As of December 31, 2015, the various series of convertible preferred stock have the following rights, preferences, and privileges):

Voting – Holders of shares of convertible preferred stock have full voting rights and powers equal to the rights and powers of holders of shares of common stock, with respect to any matters upon which holders of shares of common stock have the right to vote. Holders of shares of convertible preferred stock are entitled to the number of votes equal to the largest number of shares of common stock into which such share of convertible preferred stock could be converted at the record date for determination of the stockholders entitled to vote on such matters. Holders of shares of Series A-1, Series B-1 and Series C-1, voting together as a separate class on an as-converted basis, are entitled to elect four members of the Board. The holders of Series C-1, voting as a separate class, are entitled to elect one member of the Board. Holders of shares of common stock, voting as a separate class, are entitled to elect two members of the Board. Holders of a majority of the outstanding shares of common stock and a majority of the outstanding shares of convertible preferred stock, each voting as a separate class on an as-converted basis, are entitled to elect two members of the Board. Holders of at least 60% of the outstanding shares of convertible preferred stock and a majority of the outstanding shares of common stock, each voting as a separate class on an as-converted basis, are entitled to elect any remaining directors.

Conversion – Each share of Series C-1, Series B-1, Series A-1, and Series B is convertible at the option of the holder into one share of common stock, subject to certain adjustments for dilution, if any, resulting from future stock issuances. Each share of Series A is convertible at the option of the holder into one-fifth of a share of common stock, subject to certain adjustments for dilution, if any, resulting from future stock issuances. The outstanding shares of convertible preferred stock automatically convert into common stock at the then effective

conversion rate upon the earlier of (i) an underwritten public offering of our common stock in which aggregate proceeds are in excess of $30.0 million at a price of at least $14.00 per share, as adjusted for any recapitalization event or (ii) the election of holders of at least 60% of the outstanding shares of convertible preferred stock, voting as a separate class on an as-converted basis.

Dividends – Holders of shares of Series C-1, in preference to holders of shares of Series A-1, Series A, Series B-1, Series B, and common stock, are entitled to receive, whether or not declared by the Board, cumulative dividends at the rate of 8% of the applicable original issue price per share per annum. Such dividends accrue and are cumulative from the date of the issuance of the Series C-1. No such dividends have been declared to date. Holders of shares of Series A-1, in preference to holders of shares of Series A, Series B and common stock, are entitled to receive, whether or not declared by the Board, cumulative dividends at the rate of 8% of the applicable original issue price per share per annum. Such dividends accrue and are cumulative from the date of the issuance of the Series A-1. No such dividends have been declared to date. After payment to the holders of shares of Series C-1, holders of shares of Series B-1, in preference to holders of shares of Series A-1, Series A, Series B, and common stock, are entitled to receive, whether or not declared by the Board, cumulative dividends at the rate of 8% of the applicable original issue price per share per annum. Such dividends accrue and are cumulative from the date of the issuance of the Series B-1. No such dividends have been declared to date. After payment to the holders of shares of Series C-1 and Series B-1, holders of Series A-1, in preference to holders of shares of Series A, Series B and common stock, are entitled to receive, whether or not declared by the Board, cumulative dividends at the rate of 8% of the applicable original issue price per share per annum. Such dividends accrue and are cumulative from the date of the issuance of the Series A-1. No such dividends have been declared to date.

The Company cannot declare dividends on shares of any other class or series of capital stock unless the holders of shares of Series A-1, Series B-1 and Series C-1 first receive, on an as-converted basis, a dividend on each outstanding share of preferred stock in an amount at least equal to the product of (i) the dividend payable on each share of such class or series determined, if applicable, as if all shares of such class or series had been converted into common stock and (ii) the number of shares of common stock issuable upon conversion of a share of the applicable preferred stock, in each case calculated on the record date for determination of holders entitled to receive such dividend. As of December 31, 2015, the Company has recorded cumulative dividends on Series A-1, Series B-1 and Series C-1 of $8.7 million, $8.9 million and $2.9 million, respectively.

Liquidation – In the event of any liquidation, dissolution, winding-up, sale or merger of the Company, whether voluntarily or involuntarily, each holder of shares of Series C-1 is entitled to receive, in preference to holders of shares of Series A-1, Series A, Series B-1, Series B and common stock, a per share amount equal to the original issue price times a factor of 1.75, plus all accrued but unpaid dividends. After payment has been made to the holders of Series C-1, each holder of shares of Series B-1 is entitled to receive, in preference to holders of Series A-1, Series A, Series B and common stock, a per share amount equal to the original issue price times a factor of 1.75, plus all accrued but unpaid dividends. Each holder of shares of Series A-1 is entitled to receive, in preference to holders of shares of Series A, Series B and common stock, a per share amount equal to the original issue price, plus all accrued but unpaid dividends. Each holder of shares of Series B is entitled to receive, in preference to holders of shares of Series A and common stock, a per share amount equal to the original issue price multiplied by 75%, plus all accrued but unpaid dividends. After the above payments have been made for the full amounts to which they are entitled, any remaining assets will be distributed pro rata among holders of shares of common stock, Series A-1, Series B-1, and Series A, on an as-converted basis. The Series A has no liquidation preferences.

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

11. Common Stock

The voting, dividend, and liquidation rights of the holders of shares of common stock are subject to and qualified by the rights, powers, and preferences of the holders of shares of convertible preferred stock. Common stock has the following characteristics:

Voting – The holders of each share of common stock is entitled to one vote per share held. The holders of common stock shall be entitled to elect two members of the Board.

Dividends – Common stockholders are entitled to receive dividends, if and when declared by the Board, subject to the rights of holders of all classes of stock outstanding having priority rights as to dividends.

Liquidation – After payment to the holders of shares of preferred stock of their liquidation preferences, the holders of shares of common stock are entitled to share ratably in the Company's assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation, dissolution, or winding down of the Company or upon the occurrence of a deemed liquidation event.

The Company's reserved shares of common stock for future issuance related to potential warrant exercise, conversion of the convertible preferred stock, conversion of convertible debt and exercise of stock options are as follows:

	December 31,	
	2014	2015
Common stock issuable under Bayer warrant	127,099	277,486
Series A preferred stock	140,085	140,085
Series A-1 preferred stock	2,801,745	2,801,745
Series B preferred stock	272,240	272,240
Series B-1 preferred stock	3,031,971	3,568,020
Series C-1 preferred stock	–	6,090,461
Common stock options	1,215,160	2,956,955
Convertible notes and related accrued interest	536,049	–
Restricted stock subject to future vesting	–	14,684
Total	8,124,349	16,121,676

12. Stock-Based Compensation

In January 2007, the Board and the Company's stockholders adopted the 2007 Stock Plan (the "2007 Plan"). Under the 2007 Plan, incentive stock options, non-statutory stock options, and stock purchase rights may be granted to employees, directors, and consultants. The stock options generally vest over a four-year period, but vesting provisions can vary based on the Board's discretion and expire ten years from the date of grant. As of December 2014, the maximum number of shares issuable under the 2007 Plan was 1,220,000. During 2015 the Board increased the maximum number of shares to 3,003,374. As of December 31, 2015, there were 350,760 shares available for issuance under the 2007 Plan.

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

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 comprehensive loss as follows (in thousands):

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

As of December 31, 2015, there was $9.1 million of unrecognized compensation cost related to employee and non-employee unvested stock options and unvested restricted stock share-based compensation arrangements granted under the 2007 Plan, which is expected to be recognized over a weighted-average remaining service period of 3.2 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 that uses the 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. For options granted to employees in 2014 and 2015, the Company determined the expected term based on an average of expected terms used by a peer group of similar public companies. 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.

In determining the exercise prices for options granted, the Board has considered the fair value of the common stock as of each grant date. 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.

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,	
	2014	2015
Expected term (in years)	5.96	5.89
Volatility rate	70.36%	69.92%
Risk-free interest rate	1.91%	1.73%
Expected dividend yield	0.00%	0.00%

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

A summary of employee and non-employee option activity under the 2007 Plan 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, 2015	831,148	$ 4.99	9.0	
Granted	1,934,134	$ 8.42		
Exercised	(41,607)	$ 4.60		
Canceled or forfeited	(117,480)	$ 4.55		
Outstanding—December 31, 2015	2,606,195	$ 7.56	8.3	$ 9,463
Exercisable—December 31, 2015	723,379	$ 5.62	5.2	$ 4,142
Options vested, exercisable or expected to vest— December 31, 2015	2,526,040	$ 7.53	8.3	$ 9,256

The weighted-average grant date fair value of options granted during the years ended December 31, 2014 and 2015, was $8.92 and $5.74, respectively. The fair value is being expensed over the vesting period of the options (three to four years) on a straight-line basis as the services are being provided. There were 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. In accordance with the Company's policy, the shares were issued from a pool of shares reserved for issuance under the 2007 Plan.

The 2007 Plan allows employees to exercise unvested options in exchange for restricted common stock. Such arrangements permit the Company to subsequently repurchase such shares at the exercise price if the vesting conditions are 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, 2015, 14,684 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 $59,000 is included in other long-term liabilities in the Company's consolidated balance sheet.

In September 2014, pursuant to an option exchange program, the Company canceled 265,475 outstanding stock options for 15 employees and directors and 3 consultants. These options had been granted at exercise prices ranging from $15.38 to $47.67. The cancellation of these awards was accompanied by a concurrent grant of 265,475 replacement stock options issued with an exercise price of $6.32 per share and accounted for as a stock award modification. The incremental compensation cost was measured as the excess of the fair value of the modified grants determined over the fair value of the original award immediately before modification. The fair value of common stock used to calculate the incremental compensation cost was $6.32 per share. The unrecognized compensation cost related to the canceled awards and the incremental compensation cost arising from this modification totaled $2.1 million. The canceled and replacement awards were measured based on the fair value share price and the Black-Scholes option-pricing model assumptions at the modification date. Compensation expense of $0.5 million was recognized immediately for the portion of the expense that related to

options that were vested on the grant date. The balance of the unrecognized compensation and incremental compensation of $1.6 million will be recognized over the remaining vesting period for the respective replacement awards.

In May 2015, the vesting of certain options granted to a terminated employee was accelerated in accordance with the employment agreement, and the Company recognized $0.5 million as compensation expense due to this acceleration in vesting. In addition, as part of the termination agreement, the vesting of certain options granted was accelerated and the exercise period for all of the options was extended. This change in vesting conditions and extension of time to exercise the options was accounted for as a modification of these stock options. The aggregate increase in the fair value of the options of $0.2 million was immediately recognized as compensation expense.

13. Income Taxes

The Company has not recorded any net tax provision for the periods presented due to the losses incurred and the need for a full valuation allowance on 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,	
	2014	2015
Deferred tax assets (liabilities):		
Net operating loss carryforwards	$ 12,461	14,598
Research and development credits	1,307	1,452
Capitalized startup and research and development costs	33,107	37,641
Depreciation and amortization	(6,936)	(8,433)
Accruals	235	332
Other temporary differences	601	1,769
Deferred tax assets before valuation allowance	40,775	47,359
Valuation allowances	(40,775)	(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 $8.7 million and $6.6 million in 2014 and 2015, respectively, due to the increase in deferred tax assets, primarily due to net operating loss carryforwards and capitalized research and development costs.

As of December 31, 2015, the Company had approximately $38.6 million and $27.0 million in federal and state net operating losses, respectively, which expire at various dates from 2016 through 2035. As of December 31, 2015, the Company had federal and state research credits of $1.0 million and $0.7 million, respectively, which begin to expire in 2020.

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. As of December 31, 2014 and 2015, the Company had uncertain tax positions of $0.2 million and $0.2 million, respectively, 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. No interest or penalties were recorded for the years ended December 31, 2014 and 2015. 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, 2015, 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,	
	2014	2015
Unrecognized tax benefit—beginning of year	$ 680	$ 241
Decreases related to prior period positions	(439)	–
Unrecognized tax benefit—end of year	$ 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.

14. Commitments

License Agreements

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

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

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 December 2013, the Company entered into a 40-month lease for office space in Waltham, Massachusetts. The Company also leases office equipment, which is accounted for as a capital lease. The leased assets are included in property and equipment at cost.

Future annual minimum payments as of December 31, 2015, are as follows (in thousands):

	Operating Leases	Capital Lease Obligations
For the years ended December 31,		
2016	$ 304	$ 3
2017	266	4
2018	232	3
2019	238	–
2020	246	–
2021 and thereafter	42	–
Total minimum lease payments	$ 1,328	10
Less amounts representing interest		2
Present value of net minimum lease payments		$ 8

Rent expense for operating leases is calculated on a straight-line basis and amounted to $0.1 million for the years ended December 31, 2014 and 2015.

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 annual rent escalations 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. 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.

15. 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, 2014 and 2015, the Company had made $0 and $33,000 contributions to the plan, respectively.

SYNDAX PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (CONTINUED)

16. Related-Party Transactions

In June 2015, the Company hired a Chief Executive Officer who was also appointed as a member of the Board. This individual is also a managing director at MPM Asset Management, LLC, which holds an investment in the Company's preferred 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 10 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 $0.1 million and $0.3 million for the years ended December 31, 2014 and 2015, respectively.

17. Subsequent Events

The Company has evaluated subsequent events for financial statement purposes occurring through February 22, 2016, the date that these consolidated financial statements were originally issued, and February 24, 2016, the date on which the retrospectively revised consolidated financial statements were reissued (as a result of the reverse stock split discussed below), and determined that no additional subsequent events had occurred that would require recognition in these consolidated financial statements and that all subsequent events that require disclosure have been disclosed.

On February 24, 2016, the Company effected a 1-for-1.25 reverse stock split of the Company's common stock and convertible preferred stock. All share and per share data shown in the accompanying consolidated financial statements and related notes have been retroactively revised to reflect the reverse stock split.

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4,400,000 Shares

Common Stock

PROSPECTUS

Morgan Stanley | **Citigroup**

JMP Securities | **Oppenheimer & Co.**

March 2, 2016