Ignyta, Inc.
Form 10-K
March 14, 2017
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2016

or

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

For the transition period from _____ to _____

Commission file number: 001-36344

Ignyta, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**45-3174872**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
4545 Towne Centre Court	
San Diego, California	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

(858) 255-5959

(Registrant s Telephone Number, Including Area Code)

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.0001 per share	**Nasdaq Capital Market**

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

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes No

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

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

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

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes No

As of June 30, 2016, the last business day of the registrant s most recently completed second quarter, the aggregate market value of the registrant s common stock held by non-affiliates of the registrant was approximately $114.1 million, based on the closing price of the registrant s common stock on the Nasdaq Capital Market of $5.42 per share.

The number of outstanding shares of the registrant s common stock, par value 0.0001 per share, as of February 28, 2017 was 41,700,063.

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IGNYTA, INC.

FORM 10-K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2016

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PART I

Forward-Looking Statements and Market Data

This Annual Report on Form 10-K and the information incorporated herein by reference contain forward-looking statements that involve substantial risks and uncertainties. These forward-looking statements include, but are not limited to, statements about:

- the results of our research and development activities, including uncertainties relating to the in-license, or acquisition of potential product candidates and the preclinical and clinical testing of our product candidates;
- the stage of our product candidates presently under development;
- our ability to obtain and, if obtained, maintain regulatory approval of our current product candidates, and any of our future product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;
- our need for substantial additional funds in order to pursue our business plan and the uncertainty of whether we will be able to obtain the funding we need;
- our ability to retain or hire key scientific or management personnel;
- our ability, alone or together with partners, to validate, develop and obtain regulatory approval of companion diagnostics for our product candidates;
- our ability to protect our intellectual property rights, including patent and other intellectual property rights;
- our dependence on third-party manufacturers, suppliers, research organizations, testing laboratories and other potential collaborators;
- our ability to develop or obtain through collaborators successful sales and marketing capabilities in the future as needed;
- the size and growth of the potential markets for any of our product candidates, and the rate and degree of market acceptance of any of our product candidates;

competition in our industry;

the impact of healthcare reform legislation and other legislation pertinent to the biopharmaceutical industry; and

regulatory developments in the United States and foreign countries.

The forward-looking statements are contained principally in the sections entitled Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business. In some cases, you can identify forward-looking statements by the following words: may, will, could, would, should, expect, intend anticipate, believe, estimate, predict, project, potential, continue, ongoing or the negative of these terms comparable terminology, although not all forward-looking statements contain these words. These statements relate to future events or our future financial performance or condition and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. We discuss many of these risks, uncertainties and other factors in this Annual Report on Form 10-K in greater detail under the heading Item 1A Risk Factors.

Given these risks, uncertainties and other factors, we urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. You should read this Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995. We undertake no obligation to revise or update publicly any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business, and the markets for our product candidates, including data regarding the estimated size of markets for oncology therapeutics and the incidence of certain medical conditions, statements that certain drugs, classes of drugs or dosages are widely prescribed in the United States or other markets, statements regarding the perceptions and preferences of patients and physicians regarding certain therapies and other prescription, prescriber and patient data, as well as data regarding market research, estimates and forecasts prepared by our management. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties, and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by market research firms and other third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

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We have registered trademarks in the United States for Ignyta®, the Ignyta word mark and design, the Ignyta design, Methylome®, and Trailblaze®, and have pending trademark applications in the United States for Ignyta , the Ignyta word mark and design, the Ignyta design, Oncolome , Pharos , Trailblaze , Trailblaze Pharos and Trailblaze Pharos and design. We have registered trademarks in the European Union, or EU, for Ignyta®, the Ignyta design, Methylome®, Oncolome®, Pharos®, Trailblaze®, Trailblaze Pharos® and Trailblaze Pharos and design. All other trademarks, trade names and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners. Use or display by us of other parties trademarks, trade dress or products is not intended to and does not imply a relationship with, or endorsements or sponsorship of, us by the trademark or trade dress owner.

As used in this Annual Report on Form 10-K, unless the context indicates or otherwise requires, Ignyta, our company, we, us, and our refer to Ignyta, Inc., a Delaware corporation. On October 31, 2013, Ignyta, then known as Ignyta Operating, Inc., merged with and into IGAS Acquisition Corp., a wholly-owned subsidiary of Ignyta, Inc., or Parent, a Nevada corporation previously named Infinity Oil & Gas Company. On June 12, 2014, Parent merged with and into Ignyta, with Ignyta surviving the merger and changing its name to Ignyta, Inc.

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Item 1. Business

Business Overview

We are a biotechnology company focused on precision medicine in oncology. Our goal is not just to shrink tumors, but to eradicate residual disease the source of cancer relapse and recurrence in precisely defined patient populations. We are pursuing an integrated therapeutic, or Rx, and companion diagnostic, or Dx, strategy for treating cancer patients. Our Rx efforts are focused on in-licensing or acquiring, then developing and commercializing molecularly targeted therapies that, sequentially or in combination, are foundational for eradicating residual disease. Our Dx efforts aim to pair these product candidates with biomarker-based companion diagnostics that are designed to precisely identify, at the molecular level, the patients who are most likely to benefit from the therapies we develop.

Our current pipeline includes the following compounds:

- entrectinib, formerly called RXDX-101, an orally bioavailable, CNS-active, small molecule tyrosine kinase inhibitor directed to the TRK (tropomyosin receptor kinase) family tyrosine kinase receptors (TRKA, TRKB and TRKC), ROS1 and ALK (anaplastic lymphoma kinase) proteins, which is in a Phase 2 clinical study, two Phase 1 clinical studies in molecularly defined adult patient populations for the treatment of solid tumors, and a Phase 1/1b clinical study in pediatric patients with advanced solid tumor malignancies;

- RXDX-105, an orally bioavailable, vascular endothelial growth factor receptor, or VEGFR, -sparing, small molecule tyrosine kinase inhibitor of RET, that has achieved clinical proof-of-concept and is in an ongoing Phase 1b clinical trial;

- taladegib, an orally bioavailable, small molecule hedgehog/smoothened antagonist that has achieved clinical proof-of-concept and a recommended Phase 2 dose in a Phase 1 dose escalation trial; and

- RXDX-106, a pseudo-irreversible, small molecule inhibitor of TYRO3, AXL and MER, or collectively TAM, and c-MET that is in late preclinical development.

A kinase is an enzyme that catalyzes the transfer of phosphate groups from high-energy, phosphate-donating molecules to specific other molecules, called substrates. Tyrosine kinases transfer phosphate groups from adenosine triphosphate to cellular proteins and can function as an on/off switch for cellular functions, including cancer signaling. Cell division is partly driven by protein kinases that regulate progression through the various phases of the cell division cycle.

We acquired exclusive global development and commercialization rights to entrectinib under a license agreement with Nerviano Medical Sciences S.r.l., or NMS, that became effective in November 2013; we acquired our RXDX-105 and RXDX-106 development programs in an asset purchase transaction with Cephalon, Inc., an indirect wholly-owned subsidiary of Teva Pharmaceutical Industries Ltd., or Teva, in March 2015; and we acquired exclusive, global development and commercialization rights to taladegib under a license agreement with Eli Lilly and Company, or Lilly, in November 2015.

In May 2016, we determined to prioritize our resources and development efforts on our lead product candidate, entrectinib. In connection with this, we determined to discontinue our Spark discovery-stage program and are in

discussions with Lilly regarding the optimal path forward for taladegib in the context of our pipeline priorities. In connection with these discussions Lilly has indicated that it believes that we may not have satisfied certain of our obligations to Lilly under the license agreement, but Lilly has also indicated an interest in achieving an amicable resolution with respect to this issue and the parties are continuing discussions consistent with this desire. We also have rights to RXDX-107, a new chemical entity comprising an alkyl ester of bendamustine encapsulated in human serum albumin, or HSA, to form nanoparticles; and topical taladegib, a development program for the potential treatment of patients with superficial and nodular basal cell carcinoma. In February 2016, we announced that we had ceased all development activities relating to this program.

Our ability to identify innovative cancer targets and develop drugs against them is enabled by, and dependent on, a set of essential capabilities and the experience of our management team. The members of our team have significant experience in medicinal chemistry, lead optimization, ADME & PK (the study of absorption, distribution, metabolism, excretion, and pharmacokinetics), preclinical development and clinical development, and have collectively led or contributed to the development of multiple drugs approved by the U.S. Food and Drug Administration, or the FDA, including several cancer therapeutics. In addition, we have a laboratory accredited by the College of American Pathologists, or CAP, and certified under the Clinical Laboratory Improvement Amendments of 1988, or CLIA, and our Trailblaze Pharos assay has been granted an investigational device exemption (IDE) by the FDA. Our personnel use their expertise and our laboratory facilities with the goal of developing biomarker-based molecular assays to precisely define the patient populations in which we would test our product candidates, screen patients for enrollment in our clinical trials and potentially perform commercial companion diagnostic testing should any of our product candidates and the associated companion diagnostic obtain marketing approval.

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Cancer Background

Cancer is a heterogeneous group of diseases characterized by uncontrolled cell division and growth. Cancerous cells that arise in the lymphatic system and bone marrow are referred to as hematological tumors. Cancer cells that arise in other tissues or organs are referred to as solid tumors. Researchers believe that exposure to chemical agents, viruses and various forms of radiation can cause genetic alterations that lead to cancer. Genetic predisposition also can increase the risk of cancer in some people. Epigenetic factors are also increasingly believed to contribute to development of cancer.

Cancer is the second leading cause of death in the United States, exceeded only by heart disease. The American Cancer Society, or ACS, estimates that, in 2017, there will be approximately 1.69 million new cases of cancer and approximately 601,000 deaths from cancer in the United States. The World Health Organization estimated that 8.8 million people worldwide died of cancer in 2015. According to ACS data, breast, lung, prostate and colorectal cancer are the most prevalent cancers in the United States.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy. A cancer patient often receives treatment with a combination of these methods. Surgery and radiation therapy are particularly effective when the disease is localized. Physicians generally use drug therapy when the cancer has spread beyond the primary site or cannot otherwise be treated through surgery. The goal of drug therapy is to damage and kill cancer cells or to interfere with the molecular and cellular processes that control the development, growth and survival of cancer cells. In many cases, drug therapy entails the administration of several different drugs in combination. Over the past several decades, drug therapy has been evolving from non-specific drugs that kill both healthy and cancerous cells, to drugs that target specific molecular pathways or activating alterations involved in cancer and drugs that activate the body s immune system to destroy cancer cells.

Cytotoxic Chemotherapies. The earliest approach to pharmacological cancer treatment was to develop drugs referred to as cytotoxic drugs that kill rapidly proliferating cancer cells through non-specific mechanisms, such as deterring cell metabolism or causing damage to cellular components required for survival and rapid growth. While these drugs have been effective in the treatment of some cancers, many unmet medical needs for the treatment of cancer remain. Also, cytotoxic drug therapies act in an indiscriminate manner, killing healthy, as well as cancerous, cells. Due to their mechanism of action, many cytotoxic drugs have a narrow dose range above which the toxicity causes unacceptable or even fatal levels of damage to healthy cells and below which the drugs are not effective in eradicating cancer cells.

Targeted Therapies. The next approach to pharmacological cancer treatment was to develop drugs, referred to as targeted therapeutics, that target specific biological molecules in the human body that play a role in rapid cell growth and the spread of cancer. Targeted therapeutics are designed to preferentially kill cancer cells and spare normal cells, to improve efficacy and minimize side effects. The drugs are designed to attack either a target that causes uncontrolled growth of cancer cells or a target on which cancer cells are more dependent for their growth than normal cells. These drugs focus on eradicating processes that help the cancer cell survive. These drugs also affect oncogenes, which are the drivers or cause of the cancer itself.

Immunotherapies. Cancer cells contain mutated proteins and may overexpress other proteins normally found in the body at low levels. The immune system typically recognizes expression of these proteins, or antigens, and eliminates these cells in a highly efficient process known as immune surveillance. Cancer cells ability to evade immune surveillance is a key factor in their growth, spread, and persistence. There has been substantial scientific progress in countering these evasion mechanisms using therapies that activate the immune system to destroy tumor cells.

Strategy

We are a biotechnology company focused on precision medicine in oncology. Our goal is not just to shrink tumors, but to eradicate residual disease the source of cancer relapse and recurrence in precisely defined patient populations through the application of our integrated Rx/Dx approach. Our Rx efforts are focused on in-licensing or acquiring, then developing and commercializing molecularly targeted therapies that, sequentially or in combination, are foundational for eradicating residual disease. Our Dx efforts aim to pair these product candidates with biomarker-based companion diagnostics that are designed to precisely identify, at the molecular level, the patients who are most likely to benefit from the therapies we develop. Key elements of our strategy are to:

Employ efficient and flexible approaches to accelerate clinical development. The members of our development leadership team have diverse experience working in resource-constrained environments and have a successful history of identification, translation, development and regulatory approval of oncology products. These experiences provide our team with the knowledge to develop novel product candidates, and the ability to do so in a flexible and capital-efficient fashion. We plan to pursue indications and select specific patient populations in which activity of our product candidates can be assessed in small proof-of-concept clinical trials that may lead to accelerated clinical development. When designing clinical trials, we seek to test multiple clinical hypotheses in a single trial that can be accelerated once a signal of clinical benefit is observed. This approach may increase the likelihood of seeing results early in clinical trials with fewer patients, reducing our clinical development risk and development costs, and allowing us to potentially accelerate the development of our product pipeline.

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Test our product candidates in the patients who we believe are most likely to derive benefit. We plan to use biomarkers both to identify the drug targets that we wish to pursue, and to precisely define the patient populations in which we would test those product candidates. If our product candidates demonstrate a therapeutic benefit in those specific molecularly defined patients, then, provided that we are able to complete appropriate clinical trials and obtain regulatory approvals for those product candidates, we intend to use biomarkers to inform physicians which patients are strong candidates to be prescribed the applicable drugs.

In-license development candidates that meet our strict criteria. In seeking to expand our pipeline from time to time, we intend to impose strict criteria in order to focus on product candidates that we believe are differentiated from existing cancer therapeutics and that have well-defined, and potentially expeditious, clinical and regulatory pathways. Our criteria for selecting therapeutic product candidates for in-license or acquisition include consideration of the potential for the therapeutic to have first-in-class or best-in-class potential, and for diagnostics or specific clinical criteria that we believe would allow us to enrich our clinical study population with cancer patients who are more likely to respond to the compound.

Develop, or pursue relationships with third parties to develop, companion diagnostics to assist in identifying appropriate patients for any product candidates that we successfully commercialize. We believe that the availability of high quality companion diagnostics to help administer therapeutics to the most appropriate patients is essential. It is also important to incorporate biomarkers that we discover and utilize into a platform that can be used by regulators, physicians, payors and, most importantly, patients themselves. A companion diagnostic is a test or measurement that evaluates the presence of biomarkers in a patient, which provides information that can then assist physicians in selecting the specific drugs or treatments that may be most effective for that patient. We believe that any companion diagnostics that we develop through our laboratory facilities and related personnel, or that third parties develop through relationships with us, could be used to select patients for late stage clinical testing, to inform regulators precisely which patients should be indicated for access to the therapeutics, to advise physicians and patients which individuals are good candidates for treatment with the therapeutics, and to guide payors as to the value the therapeutics provide to well-defined patients and the circumstances under which the therapeutics should be reimbursed.

Potentially leverage partnerships to develop our product candidates. We may collaborate with third parties and partner certain rights to our product candidates as a means to accelerate their broader clinical development and maximize their therapeutic and market potential. In any such collaboration, we would likely seek to retain certain key development and commercialization rights to our product candidates as a means of retaining strategic flexibility to enable us to maximize shareholder value.

Pipeline

Consistent with our strategy, we are seeking to develop our product candidates for precise biomarker-defined patient groups. Our product candidates are at various stages of development, and we anticipate that it will be several years before any of our product candidates could be commercialized.

Entrectinib

Entrectinib is a new chemical entity that we in-licensed from NMS. Entrectinib is an orally available, CNS-active, selective tyrosine kinase inhibitor of the TRK family tyrosine kinase receptors (TRKA, TRKB and TRKC), ROS1 and ALK proteins. Entrectinib is designed as a targeted therapeutic candidate to treat patients with cancers that harbor

activating alterations to *NTRK1* (encoding TRKA), *NTRK2* (encoding TRKB), *NTRK3* (encoding TRKC), *ROS1* (encoding ROS1) or *ALK* (encoding ALK). *NTRK1*, *NTRK2*, and *NTRK3* may be collectively referred to as *NTRK*. TRKA, TRKB, and TRKC may be collectively referred to as TRK.

Rationale for Targeting TRKA, TRKB, TRKC, ROS1 and ALK

About TRK. The TRK family of tyrosine kinase receptors, which includes TRKA, TRKB and TRKC, are activated by neurotrophins, a family of nerve growth factors. The TRK family members play a key role in normal embryonic central neuronal cell development and differentiation and normal adult peripheral neuronal cell development and differentiation. Deregulated kinase activities of TRK family members occur due to gene rearrangements and translocations, mutations, overexpression and alternative splicing and are associated with a number of human neuronal and non-neuronal cancers.

About ROS1. ROS1 belongs to the insulin-receptor superfamily. Like other tyrosine kinase receptor molecules, it plays a role in relaying growth signals from the environment outside the cell into the cell s nucleus. ROS1 is one of two orphan receptor tyrosine kinase family members with no known binding ligand. Molecular rearrangements of ROS1 create fusion proteins with constitutively active kinase domains that activate downstream signaling pathways, which lead to oncogenic properties in cells, including uncontrolled proliferation and resistance to cell death with increased tumor cell survival.

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About ALK. ALK also belongs to the insulin-receptor superfamily and is related to ROS1. Aberrant ALK fusion proteins spontaneously form molecular structures that lead to self-activation and constitutive activity within cancer cells, via activation of signal transduction pathways and intracellular kinases that drive uncontrolled tumor cell growth, metabolism and survival.

Incidence of NTRK1, NTRK2, NTRK3, ROS1 and ALK Alterations; Opportunity for Entrectinib

Research to date indicates that *NTRK*, *ROS1* and *ALK* gene rearrangements and fusion proteins are most prevalent in solid tumors. Each of these genes also appears to be overexpressed in a portion of certain tumor types, though the importance of overexpression of these genes in cancer biology is not currently well understood.

- *NTRK1, NTRK2* and *NTRK3* appear to be rearranged across a range of tumor types, including non-small cell lung cancer, colorectal adenocarcinoma, salivary gland cancer, sarcoma, glioblastoma, astrocytoma, melanoma, papillary thyroid carcinoma cancer, breast cancer and cholangiocarcinoma, among other tumor types.

- *ROS1* appears to be rearranged across a range of tumor types, including non-small cell lung adenocarcinoma, colorectal adenocarcinoma, cholangiocarcinoma, sarcoma, glioblastoma, and melanoma, among other tumor types.

- *ALK* appears to be rearranged across a range of tumor types, including non-small cell lung adenocarcinoma, colorectal adenocarcinoma, cholangiocarcinoma, sarcoma, and papillary thyroid carcinoma, among other tumor types.

The potential ability of entrectinib to act as a potent inhibitor of the TRKA, TRKB, TRKC, ROS1 and ALK proteins, as well as its observed ability to be administered orally and reach systemic circulation, known as oral bioavailability, attracted us to the profile of this product candidate and support the market opportunity for the product.

Phase 1 Clinical Trials

NMS initiated a Phase 1 clinical trial in patients with solid tumors that are positive for alterations in TRKA, ROS1 or ALK. We assumed control of this trial, called the ALKA-372-001 trial, from NMS in early 2014. This open label trial is currently ongoing at two clinical sites in Italy.

In the initial two dosing schedules, patients received entrectinib for four consecutive days followed by three days without dosing. In the first such intermittent dosing schedule, patients received entrectinib in the fasted state for the first three weeks of each 28-day dosing cycle, with no dosing during the fourth week. In the second intermittent dosing schedule, patients received entrectinib in the fed state four days-on/three days-off without interruption. We are no longer enrolling patients using either intermittent dosing schedule. We are instead enrolling patients in a continuous dosing schedule, in which subjects are dosed once-daily in a fed state for each day of every 28-day dosing cycle.

In July 2014, we initiated a global Phase 1 clinical trial of entrectinib called STARTRK-1, which is the first of the Studies of Tumor Alterations Responsive to Targeting Receptor Kinases. This trial is a multicenter, single-arm, open-label clinical trial of oral entrectinib in adult patients with locally advanced or metastatic cancer confirmed to be

positive for alterations to *NTRK*, *ROS1* or *ALK*. In this trial subjects are dosed once-daily in the fed state on each day of every 28-day dosing cycle.

Both trials were designed to determine the maximum tolerated dose, or MTD, and/or recommended Phase 2 dose, or RP2D, as well as preliminary anti-cancer activity, of single agent entrectinib in patients with solid tumors with the relevant molecular alterations.

Updated results from the ALKA-372-001 and STARTRK-1 Phase 1 clinical trials were published in the journal *Cancer Discover*y in February 2017. As of the September 20, 2016, data cutoff for the publication, the findings showed:

A total of 119 patients with a range of solid tumors had been dosed across both clinical trials, with 45 patients treated at the RP2D of 600 mg, taken orally once per day (QD). The publication represented the largest published patient safety experience of any TRK inhibitor in clinical development.

Entrectinib was well tolerated, with no responding patients discontinuing the study due to adverse events, or AEs, and no evidence of cumulative toxicity, renal or hepatic toxicity, or QTc prolongation.

The majority of treatments-related AEs were Grade 1 or 2 in severity; Grade 3 events were reversible with dose modifications.

Only one Grade 4 and no treatment related Grade 5 AEs were reported across the two studies.

The most common treatment-related AEs of any grade were fatigue/asthenia, dysgeusia, parasthesias, nausea and myalgias.

25 patients across both clinical trials met the expected Phase 2 eligibility criteria, which include the presence of *NTRK1*, *NTRK2*, *NTRK3*, *ROS1* or *ALK* fusions, as opposed to other types of molecular alterations; the patient not having been previously treated with an ALK inhibitor or a ROS1 inhibitor; and treatment at or above the RP2D.

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In three patients with *NTRK1/2/3*-rearranged solid tumors (non-small cell lung cancer, or NSCLC, mammary analog secretory carcinoma, or MASC, and colorectal cancer) and with Response Evaluation Criteria in Solid Tumors, or RECIST, -measurable disease, the objective response rate, or ORR, was 100%, including complete resolution of brain metastases in the patient with NSCLC. The durations of response were 2.6 months (colorectal cancer), 4.6 months (MASC), and 15.1 months (NSCLC; patient treatment ongoing as of data cutoff date). An additional patient with an *NTRK1*-rearranged glioneuronal tumor experienced 60% reduction in tumor burden by 3-dimensional volumetric assessment (stable disease by RECIST, which is not validated for primary brain tumors).

An ORR of 86% was observed in 14 patients with *ROS1*-rearranged solid tumors (13 NSCLC patients, one melanoma patient), including two complete responses; an ORR of 85% was observed in the 13 patients with *ROS1*-rearranged NSCLC. A median duration of response of 17.4 months was seen for all ROS1-rearranged cancers, and among 13 patients with ROS1-rearranged NSCLC, the median duration of response was 17.3 months.

In seven patients with *ALK*-rearranged solid tumors, the ORR was 57%, and responses were observed in *ALK*-rearranged NSCLC, renal cell carcinoma and colorectal cancer. A median duration of response of 7.4 months was seen for ALK-rearranged cancers.

Phase 2 Clinical Trial

In September 2015, we initiated the STARTRK-2 clinical trial of entrectinib. It is a global, multicenter, open label, potentially registration-enabling Phase 2 clinical trial of entrectinib in multiple solid tumors that utilizes a basket design with screening of patient tumor samples for gene rearrangements of the relevant targets.

Diagnostic Technologies for Patient Identification

Multiple diagnostic technologies are available for measuring alterations in *NTRK1*/2/3, *ROS1* and *ALK*. There is an FDA-approved fluorescence in situ hybridization (FISH) test for measuring ALK translocations (Vysis, manufactured by Abbott Molecular). There is also a commercially available FISH test for measuring ROS1 translocations. In addition, ALK and ROS1 protein expression levels can also be measured by immunohistochemistry (IHC) using commercially available antibodies, including the FDA-approved companion diagnostic assay for ALK from Ventana Medical Systems, Inc. Finally, several commercial, as well as academic, groups offer next generation sequencing-based methods for the detection of sequence mutations and gene translocations of *NTRK1*, *NTRK2*, *NTRK3*, *ROS1* and *ALK*.

We have evaluated each of these candidate diagnostic approaches, and we have developed a proprietary, RNA-based companion diagnostic next-generation screening, or NGS, assay, called Trailblaze Pharos, to be performed in our CAP-accredited and CLIA-certified diagnostic laboratory. In August 2016, the FDA approved an investigational device exemption, or IDE, for our Trailblaze Pharos assay which is intended for use in identifying patients, including those who are treatment-naïve, who have solid tumors with *NTRK1/2/3*, *ROS1*, or *ALK* gene rearrangements leading to fusion proteins, to determine eligibility for enrollment into the global STARTRK-2 clinical trial. In November 2016, the FDA also granted our request to review our Trailblaze Pharos companion diagnostic test service under the Expedited Access Pathway, or EAP, program. Our diagnostic development team is also building upon our Trailblaze platform to detect molecular alterations of interest for our other targeted programs.

RXDX-105

RXDX-105 is a new chemical entity that we acquired in 2015 from Teva. RXDX-105 is an orally bioavailable, small molecule tyrosine kinase inhibitor with potent activity against RET that spares vascular endothelial growth factor, or VEGFR. We believe this program enables us the potential for a first-in-class and best-in-class opportunity in RET-driven solid tumors.

Rationale for Targeting RET

About RET. The RET proto-oncogene is a receptor tyrosine kinase that sits at the cell surface. When activated, it initiates downstream cellular proliferation and survival pathways such as MAP kinase, PI3 kinase and PLC gamma. RET can be prone to gene rearrangements and other activating mutations that can cause autophosphorylation and become oncogenic drivers by constitutively activating these downstream signaling pathways.

Phase 1/1b Clinical Trial

Teva initiated a Phase 1/1b dose escalation clinical trial which was designed to determine the MTD and/or RP2D, as well as preliminary anti-cancer activity, of single agent RXDX-105 in patients with advanced or metastatic solid tumors that were not selected based on any molecular alteration. We assumed control of this trial in mid-2015.

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We announced data from this ongoing clinical trial in December 2016 at the 2016 EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium. As of the November 2016 data cut-off for the presentation, the findings showed:

- A total of 91 patients with a range of solid tumors were dosed in the clinical trial, with 55 patients treated in the Phase 1 study and 36 patient treated in the Phase 1b study.

- RXDX-105 continues to demonstrate a safety profile similar to what has been previously reported.

  - The most frequent (>10% incidence) treatment-related AEs were rash, fatigue, diarrhea, nausea, hypophosphatemia, vomiting, muscle spasms and decreased appetite. The majority of treatment-related AEs were Grade 1 or 2, and were reversible with dose modification. The most common Grade 3 treatment-related AEs were rash, hypophosphatemia, and an increase in alanine aminotransferase, or ALT.

  - One patient experienced a Grade 3 drug reaction with eosinophilia and systemic symptoms, in which the patient recovered with drug discontinuation. One patient experienced Grade 3 rash complicated by fatal alveolar hemorrhage.

  - Toxicities commonly associated with VEGFR inhibition, such as hypertension, hypothryroidism, proteinuria, and neutrotoxicity, were rarely observed.

- Of the 36 patient treated in the Phase 1b study, 35 had RET or BRAF molecular alterations.

- Nine RET inhibitor-naïve patients with RET fusion-positive tumors were treated at a daily dose of 275 mg or 350 mg in the fed state, and were evaluable for response.

- A preliminary ORR of 56% was observed in patients with RET fusion-positive solid tumors who were RET inhibitor-naïve (five out of nine treated patients had a RECIST response). Of the five patients demonstrating a RECIST response, one patient with metastatic colorectal cancer (mCRC) achieved a complete response; three patients, all with NSCLC, achieved a partial response; and one patient with NSCLC had an unconfirmed partial response.

  - Among the seven patients with RET fusion-positive NSCLC who were RET inhibitor- naïve, three achieved a partial response and one achieved an unconfirmed response (a second scan had not been obtained at the date of the data cutoff), for a preliminary ORR of 57%.

Duration of response to RXDX-105 ranged from 2+ to 7+ months, with all responder patients currently continuing on treatment in active response; median duration of response, therefore, has not yet been determined.

Additionally, a previously disclosed Phase 1 patient with RET-mutated M918T medullary thyroid cancer had a confirmed partial response and continues on treatment after 10 cycles.

Among the remaining patients treated in Phase 1b who were either RET fusion-positive and received prior RET inhibitor treatments, or had BRAF molecular alterations, durable disease control but no objective responses have been observed to date.

These data demonstrated that RXDX-105 was active across a range of different histologies, with confirmed RECIST responses observed in medullary thyroid cancer, NSCLC, and mCRC, and across a range of RET molecular alterations, including the M918T point mutation, and CCDC6-, EML4-, and PARD3-RET fusions.

Taladegib

Taladegib is a new chemical entity to which we acquired rights from Lilly in 2015. Taladegib is an orally available, small molecule hedgehog/smoothened antagonist that has achieved clinical proof-of-concept and a recommended Phase 2 dose in a Phase 1 dose escalation trial.

Rationale for Targeting Hedgehog

The hedgehog pathway is a cell signaling pathway that transmits information to embryonic cells required for proper development. Dysregulated signaling can arise from molecular alterations at multiple nodes in the pathway, which can lead to uncontrolled cell growth in multiple solid tumor types. Regulation of the pathway can be affected through modulation of multiple receptors, including the G protein-coupled receptor smoothened.

Phase 1 Clinical Trial

Lilly initiated a Phase 1 clinical trial of oral taladegib in patients with solid tumors. This multicenter, dose escalation clinical trial was designed to determine the MTD and RP2D, as well as preliminary anti-cancer activity, of single agent oral taladegib in patients with advanced or metastatic solid tumors. Patients were dosed once daily for 28 days. There were three phases to the study: a dose escalation phase in patients with advanced cancer, a dose confirmation phase in patients with advanced cancer, and a disease expansion cohort in patients with locally advanced or metastatic basal cell carcinoma.

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Lilly presented interim results from this clinical trial in November 2015 at the 2015 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. As of the data cut-off for the presentation, the findings showed:

A total of 84 patients with a range of solid tumors had been dosed, 47 of whom had advanced or metastatic basal cell carcinoma.

The most frequent (>10% incidence) treatment-related AEs were dysgeusia, fatigue, nausea, muscle spasms and decreased appetite. Most toxicities were Grade 1 or 2, with 18 reported Grade 3 AEs. There were no Grade 4 or Grade 5 AEs reported. Dose limiting toxicity was seen at 600 mg, and the maximum tolerated dose was determined to be 400 mg, once daily.

Among patients with advanced or metastatic basal cell carcinoma, the overall response rate in patients who were hedgehog inhibitor naïve was 69%, based on 11 responses out of 16 patients. The overall response rate in patients who had previously received hedgehog inhibitor therapy was 38%, based on 11 responses out of 29 evaluable patients. Taking into account patients with stable disease, the percentage of patients who received clinical benefit from taladegib treatment was 100% in the hedgehog inhibitor naïve patient subset and approximately 90% in the previously hedgehog inhibitor treated patient subset.

In May 2016, we determined to prioritize our resources and development efforts on our lead product candidate, entrectinib, and are in discussions with Lilly regarding the optimal path forward for taladegib in the context of our pipeline priorities. In connection with these discussions Lilly has indicated that it believes that we may not have satisfied certain of our obligations to Lilly under the license agreement, but Lilly has also indicated an interest in achieving an amicable resolution with respect to this issue and the parties are continuing discussions consistent with this desire.

RXDX-106

RXDX-106 is a small molecule, pseudo-irreversible inhibitor of TYRO3, AXL and MER, or collectively TAM, and c-MET that is in late preclinical development.

Rationale for Targeting TAM and c-MET

About TAM. Numerous studies have shown that the TAM receptors play a critical, dual regulatory role in cancer. Aberrantly elevated TAM signaling is associated with cancer progression, metastasis and drug resistance. At the same time, TAM receptors in diverse immune cells, such as macrophages, T cells, NK cells and dendritic cells, are key negative regulators of both innate and acquired immunity. Thus, targeted inhibition of TAM receptors has emerged as a potential novel strategy for cancer treatment by not only impeding the tumorigenic, metastatic, and chemo-resistant capabilities of the tumor cells, but also by activating innate and adaptive anti-tumor immune responses.

About c-MET. The c-MET pathway plays an important role in cancer development, progression and resistance to anti-EGFR and other targeted therapies. Particularly, molecular alterations that result in MET exon 14 skipping are found in lung cancer and other cancer types and shown to confer sensitivity to MET inhibition.

License Agreements

November 2013 Agreement with NMS

We entered into a license agreement with NMS on October 10, 2013, which was amended on October 25, 2013, became effective on November 6, 2013, and was amended December 12, 2014. The agreement grants us exclusive global rights to develop and commercialize entrectinib, as well as a second product candidate, RXDX-102. As a result of the clinical results relating to entrectinib that we have seen to date, we designated RXDX-102 as a back-up compound to entrectinib. Accordingly, we will not devote further development resources to RXDX-102.

Our development rights under the license agreement are exclusive for the term of the agreement with respect to entrectinib and RXDX-102 and also, as to NMS, are exclusive for a five-year period with respect to any product candidate with activity against the target proteins of entrectinib and RXDX-102, and include the right to grant sublicenses. We are obligated under the license agreement to use commercially reasonable efforts to develop and commercialize a product based on either or both of entrectinib and RXDX-102, at our expense.

Under the terms of the license agreement, on November 6, 2013, we issued to NMS a warrant to acquire up to 16,667 shares of our common stock, which has an exercise price of $6.00 per share and is exercisable at any time at the option of the holder until November 6, 2018. The terms of the license agreement also provided for an up-front payment to NMS of $7.0 million. When and if commercial sales of a product based on either or both of entrectinib or RXDX-102 begin, we will be obligated to pay NMS tiered royalties ranging from a mid-single digit percentage to a low double digit percentage (between 10% and 15%) of our net sales, depending on the amount of our net sales, with standard provisions for royalty offsets to the extent we obtain any rights from third

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parties to commercialize the product. The license agreement also requires that we make development and regulatory milestone payments to NMS of up to $105.0 million in the aggregate if specified clinical study initiations and regulatory approvals are achieved across multiple products or indications. Pursuant to the December 2014 amendment to the agreement, we paid the initial milestone payment of $10.0 million to NMS in December 2014.

The license agreement with NMS will remain in effect until the expiration of all of our royalty and sublicense revenue payment obligations to NMS. Those payment obligations commence after the first commercial sale of a product covered by the claims of any patent subject to the license agreement, and continue, on a product-by-product and country-by-country basis, through the longer of (i) the expiration of the last-to-expire valid patent in such country with claims covering such product or (ii) 10 years after the first commercial sale of such product in such country. The license agreement may be terminated under the following circumstances: (a) prior to the first commercial sale of a product covered by the agreement, if we provide NMS with 60 days prior written notice of our termination of the agreement, (b) after the first commercial sale of any product covered by the agreement, if we provide NMS with three months prior written notice of our termination of the agreement (in which case NMS may then accelerate the effective date of the termination to not less than 30 days after our notice), or (c) upon a material breach by either party under the agreement, which breach is not cured within 30 days with respect to payment defaults or within 60 days with respect to any other breach (which cure period may be extended to up to 120 days for breaches other than payment defaults). As a result, if we fail to meet our payment or other obligations under the license agreement and are unable to cure any such failure within the specified cure periods, NMS could terminate the license agreement and we would lose our rights to entrectinib and RXDX-102.

Agreement with Daiichi Sankyo

In connection with our March 2015 asset acquisition from Teva, we assumed all rights and obligations under the collaboration agreement dated November 3, 2006, as amended April 17, 2009, between Cephalon, Inc. and Daiichi Sankyo Company, Limited, or Daiichi Sankyo, as successor-in-interest to Ambit Biosciences Corporation. The collaboration was for the purpose of identifying and developing clinical candidates that demonstrate activity towards the two designated target kinases of the collaboration: the BRAF kinase and the AXL kinase. Under the agreement, both parties contributed certain intellectual property to the collaboration and agreed to a period of exclusivity during which neither party would engage in any research related to a collaboration target compound with any third-party. The collaboration portion of the agreement ended in November 2009, but the agreement remains in effect on a product-by-product, country-by-country basis until all royalty obligations expire. Both parties have a right to terminate the agreement if the other party enters bankruptcy or upon an uncured breach by the other party. We may also terminate the agreement in our discretion upon 90 days written notice to Daiichi Sankyo.

We are solely responsible for worldwide clinical development and commercialization of collaboration compounds, which include RXDX-105 and RXDX-106, subject to the option of Daiichi Sankyo, exercisable during certain periods following completion of the first proof-of-concept study in humans and only with our consent, to co-develop and co-promote RXDX-105. If we decide to discontinue development of the RXDX-105 program, we must give written notice to Daiichi Sankyo, which will have the right to assume control of that program, subject to diligence obligations and payment of the milestones and royalties to us that would otherwise have been paid to Daiichi Sankyo had we maintained responsibility for the program.

The agreement requires us to make development, regulatory and sales milestone payments to Daiichi Sankyo of up to $44.5 million in the aggregate for RXDX-105, and up to $47.5 million in the aggregate for RXDX-106. When and if commercial sales of a product based on either of RXDX-105 or RXDX-106 begin, we will be obligated to pay Daiichi Sankyo tiered royalties ranging from a mid-single digit percentage to a low double digit percentage of net sales, depending on annual amounts of net sales, with standard provisions for royalty offsets to the extent we are required to

obtain any rights from third parties to commercialize either RXDX-105 or RXDX-106. Royalties are payable to Daiichi Sankyo on a product-by-product, country-by-country basis beginning on the date of the first commercial sale in a country and ending on the later of 10 years after the date of such sale in that country or the expiration date of the last to expire patent subject to the agreement covering the product in that country.

Agreement with Lilly

On November 6, 2015, we entered into a license, development and commercialization agreement with Lilly, pursuant to which we received exclusive, global rights to develop and commercialize pharmaceutical products under certain licensed technology, including the oral and topical forms of the product candidate taladegib. We granted back to Lilly an exclusive license to develop and commercialize pharmaceutical products comprising taladegib in combination with certain other molecules.

We are obligated under the agreement to use commercially reasonable efforts to develop and commercialize pharmaceutical products utilizing the licensed technology, at our expense.

The agreement provided for an up-front payment by us to Lilly of $2.0 million and the issuance by us to Lilly in a private placement of 1,213,000 unregistered shares of our common stock. When and if commercial sales of products we develop under the license begin, we will be obligated to pay Lilly a mid-single digit royalty based on net sales. When and if commercial sales of combination products developed by Lilly under the grant-back license begin, Lilly will be obligated to pay us a royalty of net sales. Both parties royalty obligations are subject to standard provisions for royalty offsets to the extent a party is required to obtain any rights from third

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parties to commercialize the applicable products, or in the event of loss of exclusivity or generic competition. The agreement also requires that we make development and sales milestone payments to Lilly of up to $38.0 million. We may elect to pay a portion of such amounts by issuing to Lilly shares of our common stock in a private placement, subject to certain conditions.

Unless terminated earlier, the agreement will remain in effect, on a country-by-country and product-by-product basis, until the parties royalty obligations end. Each party has a right to terminate the agreement if the other party enters bankruptcy, upon an uncured breach by the other party or if the other party challenges its patents relating to the licensed technology.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. While we believe that our technology, development experience, scientific knowledge and strategies provide us with competitive advantages, we face competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions. Any product candidates that we are able to successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future. Our competitors may develop or market products or other novel technologies that are more effective, safer, more convenient or less costly than any that may be commercialized by us, or may obtain regulatory approval for their products more rapidly than we may obtain approval for ours.

The acquisition or licensing of pharmaceutical products is also very competitive, and a number of more established companies, some of which have acknowledged strategies to license or acquire products and many of which are bigger than us and have more institutional experience and greater cash flows than we have, may have competitive advantages over us, as may other emerging companies taking similar or different approaches to product licenses and/or acquisitions. In addition, a number of established research-based pharmaceutical and biotechnology companies may acquire products in late stages of development to augment their internal product lines, which may provide those companies with an even greater competitive advantage.

Many of our competitors will have substantially greater financial, technical and human resources than we have. Mergers and acquisitions in the pharmaceutical industry may result in even more resources being concentrated in some of our competitors. Competition may increase further as a result of advances made in the commercial applicability of technologies and greater availability of capital for investment in these fields. Our success will be based in part on our ability to build, obtain regulatory approval for and market acceptance of, and actively manage, a portfolio of drugs that addresses unmet medical needs and creates value in patient therapy.

We compete in the segments of the pharmaceutical, biotechnology and other related markets that pursue precision medicine approaches to combatting activating molecular alterations in cancer. There are a number of other companies presently working to develop therapies for cancer in the field of precision medicines, including divisions of large pharmaceutical companies, and pharmaceutical and biotechnology companies of various sizes.

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, or a combination of such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these

approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payers. As a result, obtaining market acceptance of, and a gaining significant share of the market for, any of our product candidates that we successfully introduce to the market will pose challenges.

In addition to currently marketed therapies, there are also a number of medicines in late stage clinical development to treat cancer. These medicines in development may provide efficacy, safety, convenience and other benefits that are not provided by currently marketed therapies and may not be provided by any of our current or future product candidates. As a result, they may provide significant competition for any of our product candidates.

With respect to entrectinib, we are aware that Loxo Oncology is developing larotrectnib (LOXO-101) for patients with TRK-positive solid tumors, and has initiated a Phase 2 basket trial in adult cancer patients whose tumors harbor TRK fusions and a Phase 1/1b trial in pediatric cancer patients. We are also aware of three agents that have been approved by the FDA for ALK-positive NSCLC Pfizer s Xalkori®/crizotinib, Novartis Zykadia®/ceritinib and Roche s Alecensa®/alectinib. Alectinib is also approved for this indication in Japan. In addition, we are aware that Pfizer s Xalkori®/crizotinib has also been approved by the FDA for ROS1-positive NSCLC.

With respect to taladegib, we are aware of two agents that have been approved by the FDA to treat basal cell carcinoma and are designed to selectively inhibit the hedgehog pathway by binding the smoothened protein: Genentech s Erivedge®/vismodegib and Novartis Odomzo®/sonidegib.

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We are also aware of several other products in development targeting TRKA, TRKB, TRKC, ROS1, ALK, Hedgehog/Smoothened, RET, TYRO3, AXL, MER and/or c-MET for the treatment of cancer, some of which may be in a more advanced stage of development than our product candidates. There are also many other compounds directed to other molecular targets that are in clinical development by a variety of companies to treat cancer types that we may choose to pursue with our programs.

Commercialization

We have not yet established significant sales, marketing or product distribution infrastructure. For any of our product candidates for which we may in the future receive marketing approvals, we may seek to commercialize the product ourselves or to avail ourselves of commercial capabilities through one or more collaborations. In any such collaboration, we would likely seek to retain certain commercialization rights to our product candidates as a means of retaining strategic flexibility to enable us to maximize shareholder value.

To the extent that we internally develop and obtain regulatory approval for commercial companion diagnostics for use with our therapeutic products, we may market and sell those diagnostics through our own sales and marketing teams or we may seek a commercialization partner. To the extent we collaborate in the future with any third parties on the development of any commercial companion diagnostics for use with our therapeutic products, such third parties will most likely hold the commercial rights to those diagnostic products. We expect that we would coordinate closely with any future diagnostic collaborators in connection with the marketing and sale of such diagnostic products and our related therapeutic products.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture of any products that we may commercialize. We have a limited number of supply arrangements for entrectinib, and we are currently reliant on a single contract manufacturer for the clinical supply of RXDX-105. In addition, we have only a limited clinical supply of taladegib, and we must seek to establish clinical supply agreements with third parties for future supplies. We do not currently have arrangements in place for commercial supply of bulk drug substance or drug products. For all of our product candidates, we plan to identify and qualify manufacturers to provide the active pharmaceutical ingredient and fill-and-finish services prior to submission of a new drug application, or NDA, to the FDA.

We believe that all of our product candidates can be manufactured in reliable and reproducible synthetic processes from readily available materials. We believe that the chemistry is amenable to scale-up and does not require unusual or expensive equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

We generally expect to rely on third parties for the manufacture of any companion diagnostics we or our collaborators may develop.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our product candidates and our core technologies, to operate without infringing any intellectual property rights of others and to prevent others from infringing our proprietary or intellectual property rights. We expect that we will seek to protect our proprietary and intellectual property position by, among other methods, licensing or filing our

own U.S. and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position, which we generally seek to protect through trade secret law and contractual obligations with third parties.

We currently, and expect that we will continue to, file or license patent applications directed to our key product candidates in an effort to establish intellectual property positions regarding the new chemical entities utilized in these product candidates, as well as uses of these chemical entities in the treatment of various cancers. We also may seek patent protection, if available, with respect to biomarkers and diagnostic methods that may be useful in selecting the right patient population for use of any of our product candidates.

Our license agreements relating to our entrectinib, RXDX-105, and taladegib development programs grant us exclusive, worldwide licenses under a portfolio of patents and patent applications directed to the licensed development programs. We own the rights to composition of matter patents and patent applications directed to our RXDX-106 and RXDX-107 programs. The composition of matter patents in the United States expire in 2029 for the issued patent relating to entrectinib, in 2030 for the issued patent relating to RXDX-105, in 2032 for the issued patent relating to RXDX-106, in 2033 for the issued patent relating to RXDX-107, and in 2031 for the issued patent relating to taladegib.

We plan to continue to expand our intellectual property portfolio by filing patent applications in the United States and internationally for novel compositions of matter that we may develop covering our compounds, the chemistries and processes for manufacturing these compounds, the use of these compounds in a variety of therapies and potentially for the use of biomarkers for patient selection for

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these compounds. Of course, these or other patent applications that we may file or license from third parties may not issue as patents, and any issued patents may have claims that are substantially more limited than the patents disclosure. Any issued claims may be of a scope that may reduce their value and/or may be challenged, invalidated or circumvented. See Risk Factors Rights Related to Our Intellectual Property.

In addition to patents, we have registered trademarks in the United States for Ignyta®, the Ignyta word mark and design, the Ignyta design, Methylome®, and Trailblaze®, and have pending trademark applications in the United States for Ignyta , the Ignyta word mark and design, the Ignyta design, Oncolome , Pharos , Trailblaze , Trailblaze Pharos and Trailblaze Pharos and design. We have registered trademarks in the European Union, or EU, for Ignyta®, the Ignyta design, Methylome®, Oncolome®, Pharos®, Trailblaze®, Trailblaze Pharos® and Trailblaze Pharos and design. We also rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our collaborators, scientific advisors, employees and consultants, and invention assignment agreements with our employees and selected consultants, scientific advisors and collaborators. The confidentiality agreements are designed to protect our proprietary information and, in the case of agreements or clauses requiring invention assignment, to grant us ownership of technologies that are developed through a relationship with a third party.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of pharmaceutical products, such as those we are developing.

United States Drug Approval Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, approval process or after approval, may subject an applying company to a variety of administrative or judicial sanctions.

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

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with good laboratory practice, or GLP, regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- approval of each phase of the proposed clinical trials and related informed consents by an institutional review board, or IRB, at each clinical site where such trial will be performed;

performance of adequate and well-controlled human clinical trials in accordance with good clinical practice, or GCP, standards and regulations to establish the safety and efficacy of the proposed drug for each indication;

submission to the FDA of an NDA;

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the drug s identity, strength, quality and purity; and

FDA review and approval of the NDA.

Preclinical Studies and IND

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for AEs and, in some cases, to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive AEs and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

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Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the safety and effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. In addition, an IRB at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. In addition, a sponsor must provide information regarding most clinical trials to be disclosed on http://clinicaltrials.gov, a website maintained by the National Institutes of Health.

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

Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.

Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3: The drug is administered to an expanded patient population in adequate and well-controlled clinical trials to generate sufficient data to statistically confirm the efficacy and safety of the product for approval for specified indications, to establish the overall risk-benefit profile of the product and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA, and more frequently if serious AEs occur. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution 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.

Pursuant to the 21st Century Cures Act, which was enacted on December 13, 2016, the manufacturer of an investigational drug for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access. This requirement applies on the later of 60 days after the date of enactment or the first initiation of a Phase 2 or Phase 3 trial of the investigational drug.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product s chemistry, manufacture, controls and proposed labeling,

among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is subject to a substantial application user fee.

The FDA generally conducts a preliminary review of all NDAs to determine if they are sufficiently complete to permit substantive review within the first 60 days after submission before accepting them for filing. The FDA may request additional information in connection with this preliminary review rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is subject to further review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review of NDAs. Under these goals, the FDA has committed to review most such applications for non-priority products within 10 months, and most applications for priority review products, that is, drugs that the FDA determines represent a significant improvement over existing therapy, within six months. The FDA may also refer applications for novel drugs or 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. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA is not required to adhere its review time goals, and its review could experience delays that cause those goals to not be met.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. In addition, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and integrity of the clinical data submitted.

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The testing and approval process for each product candidate requires substantial time, effort and financial resources, and each may take many years to complete. Data obtained from preclinical and clinical activities are not always conclusive and may be susceptible to varying interpretations, which could delay, limit or prevent regulatory approval. The FDA may not grant approval of an application for a product candidate on a timely basis, or at all. Further, applicants often encounter difficulties or unanticipated costs in their efforts to develop product candidates and secure necessary governmental approvals, which could delay or preclude the marketing of those products.

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

Programs for Expedited Review and Approval

The FDA has developed certain programs and designations that enable NDAs for product candidates meeting specified criteria to be eligible for certain expedited review and approval processes such as fast track designation, priority review, accelerated approval, and breakthrough therapy designation. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Fast Track Designation. The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and that demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new product candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the submission of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor s request.

In addition to other benefits, such as the ability to use surrogate endpoints (see the description of surrogate endpoints under Accelerated Approval below) and have greater interactions with the FDA, the FDA may initiate review of sections of a fast track product s NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA s review time goal for a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Priority Review. Under FDA policies, a product candidate may be eligible for priority review, or review generally within a six-month timeframe from the time a complete application is accepted for filing. Products regulated by the FDA s Center for Drug Evaluation and Research are eligible for priority review if they provide a significant improvement compared to marketed products in the treatment, diagnosis or prevention of a disease. A fast track designated product candidate would ordinarily meet the FDA s criteria for priority review.

Under the FDA s Rare Pediatric Disease Priority Review Voucher program, upon the approval of a qualifying NDA or biologics license application, or BLA, for the treatment of a rare pediatric disease, the sponsor of such application

would be eligible for a Pediatric Disease Priority Review Voucher that can be used to obtain priority review for a subsequent NDA or BLA. The FDA defines a rare pediatric disease as a disease that (1) is a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents and (2) is a rare disease or condition within the meaning of the Orphan Drug Act (i.e., it affects fewer than 200,000 individuals in the U.S.). The FDA has granted us rare pediatric disease designation for entrectinib for the treatment of neuroblastoma.

Accelerated Approval. Under the FDA s accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon 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. In clinical trials, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or sooner than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to validate the surrogate endpoint or otherwise

confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough Therapy Designation. A sponsor can request designation of a product candidate as a breakthrough therapy. 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, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Additional Regulatory Designations and Alternative Approval Pathways

In addition to the expedited review and approval programs and designations, the FDA also recognizes certain other designations and alternative approval pathways that afford certain benefits, such as the orphan drug designation and alternative types of NDAs under the Hatch-Waxman Act.

Orphan Drugs. Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. The FDA has granted us orphan drug designation for entrectinib for the treatment of neuroblastoma and for the treatment of TRKA-positive, TRKB-positive, TRKC-positive, ROS1-positive or ALK-positive non-small cell lung cancer and colorectal cancer. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

The first NDA applicant to receive FDA approval for a particular active moiety to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product and for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same orphan indication, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity, such that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA application user fee.

The Hatch-Waxman Act: Abbreviated New Drug Applications. In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant s product or a method of using the product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. A drug listed in the Orange Book may, in turn, function as a reference listed drug, or RLD, and be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. Generally, an ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths, dosage form and route of administration as the RLD and has been shown to be bioequivalent through *in vitro* or *in vivo* testing or otherwise to the RLD. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their proposed ANDA drug product, other than the requirement for bioequivalence

testing. Drugs approved in this way are commonly referred to as generic equivalents to the RLD, and can be and are often substituted by pharmacists under prescriptions written for the RLD.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the RLD in the Orange Book, except for patents covering methods of use of the RLD for which the ANDA applicant is not seeking FDA approval. Specifically, the applicant must certify with respect to each Orange Book-listed patent that:

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

A certification that the proposed ANDA product will not infringe the patents listed for the RLD or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the ANDA applicant does not challenge the Orange Book-listed patents or indicate that it is not seeking FDA approval of a method of use covered by a patent listed in the Orange Book for the RLD, the ANDA application will not be approved until all the Orange Book-listed patents for the RLD have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA with respect to one or more patents listed in the Orange Book for the RLD, the ANDA applicant must also send notice of the Paragraph IV certification to the NDA holder for the RLD and

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the owner(s) of the Orange Book-listed patents for the RLD after the ANDA has been accepted for filing by the FDA. The NDA and patent owners may then initiate a patent infringement lawsuit against the ANDA applicant in response to the notice of the Paragraph IV certification. The filing of such a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV notice automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA also will not be approved until any applicable non-patent exclusivity periods, such as exclusivity for obtaining approval of a new chemical entity, applicable to the RLD have expired. Federal law provides a period of five years following FDA approval of a RLD containing a new active moiety, during which time an ANDA for a generic version of the RLD cannot be filed with the FDA, unless the ANDA contains a Paragraph IV certification to an Orange Book-listed patent for the RLD, in which case the ANDA may be filed with the FDA four years following approval of the RLD. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an ANDA if the RLD contains a previously approved active moiety and the application contained data from new clinical studies (other than bioavailability studies) conducted or sponsored by the sponsor that were essential to the approval of the application. This three-year exclusivity period often protects new drug products that contain a previously approved active moiety, such as a new dosage form, route of administration, combination or indication. Under the Best Pharmaceuticals for Children Act, federal law also provides that periods of patent and non-patent marketing exclusivities listed in the Orange Book for a RLD may be extended by six months if the NDA sponsor conducts pediatric studies identified by the FDA in a written request. If such a written request is issued by the FDA, the FDA must grant pediatric exclusivity no later than six months prior to the date of expiration of patent or non-patent exclusivities in order for the six-month pediatric extension to apply to those exclusivity periods.

The Hatch-Waxman Act: Section 505(b)(2) New Drug Applications. Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on the FDA s prior findings of safety and efficacy for an approved product that is a RLD, or published literature, in support of its application.

Section 505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of drugs containing previously approved active moieties. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on the FDA s previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all or some of the label indications for which the RLD has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

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

Combination Products

The FDA regulates combinations of products that cross FDA centers, such as drug, biologic or medical device components that are physically, chemically or otherwise combined into a single entity, as a combination product. The FDA center with primary jurisdiction for the combination product will take the lead in the premarket review of the product, with the other center consulting or collaborating with the lead center. The 21st Century Cures Act, or Cures Act, amended the provisions of the FDCA relating to the regulation of combination products to, among other things, require the FDA to conduct the premarket review of any combination product under a single application whenever appropriate.

In practice, the FDA s Office of Combination Products, or OCP, determines which center will have primary jurisdiction for the combination product based on the combination product s primary mode of action. A mode of action is the means by which a product achieves an intended therapeutic effect or action. The primary mode of action is the mode of action that provides the most important therapeutic action of the combination product, or the mode of action expected to make the greatest contribution to the overall intended therapeutic effects of the combination product.

Often it is difficult for the OCP to determine with reasonable certainty the most important therapeutic action of the combination product. In those difficult cases, the OCP will consider consistency with other combination products raising similar types of safety and effectiveness questions, or which center has the most expertise to evaluate the most significant safety and effectiveness questions raised by the combination product.

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If a combination product sponsor disagrees with OCP s primary mode of action determination, the Cures Act permits the sponsor to request that FDA provide a substantive rationale for its determination. The sponsor can then propose one or more studies to establish the relevance of the chemical action in achieving the product s primary mode of action and FDA and the sponsor will collaborate to reach agreement on the design of such studies within 90 calendar days. If the sponsor conducts the agreed-upon studies, FDA must consider the resulting data when reevaluating the product s primary mode of action.

Post-Market Drug Regulation

If the FDA approves a drug product for commercial marketing, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug s safety and/or other factors after approval, require testing and surveillance programs to monitor the product after commercialization and/or patients using the product for observation of the product s long-term effects, or impose other conditions, including distribution restrictions or other risk management mechanisms, including Risk Evaluation and Mitigation Strategies, or REMS, which can materially affect the potential market and profitability of the product. Any approved product is also subject to requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion, labeling, and reporting of adverse experiences with the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and re-approval.

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

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

- restrictions on the marketing or manufacturing of the product, product recalls or complete withdrawal of the product from the market;

- fines, warning or untitled letters or holds on post-approval clinical trials;

refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;

product seizure or detention, or refusal to permit the import or export of products; or

consent decrees, injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off label uses, and a company that is found to have improperly promoted off label uses may be subject to significant liability.

FDA Regulation of Companion Diagnostics

We may seek to develop or seek to partner with third parties to develop *in vitro* companion diagnostics for use in selecting the patients that we believe will respond to our drug therapeutics. Companion diagnostics are regulated by the FDA as medical devices.

In August 2014 the FDA issued guidance that addresses issues critical to developing *in vitro* companion diagnostics. The guidance states that if safe and effective use of a therapeutic product depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic product. In July 2016, the FDA issued a draft guidance intended to assist sponsors of the drug therapeutic and *in vitro* companion diagnostic device on issues related to co-development of the products.

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The FDA generally requires *in vitro* companion diagnostics intended to select the patients intended to receive a cancer treatment to obtain approval of a pre-market application, or PMA approval, for that diagnostic simultaneously with approval of the drug.

Medical Device Approval Pathways

To be commercially distributed in the United States, a medical device, including an *in vitro* diagnostic, or IVD, must receive either 510(k) clearance, de novo authorization, or PMA approval from the FDA prior to marketing. There are three classes of medical devices recognized by the FDA, Class I (low risk), Class II (moderate risk), and Class III (high risk). Class III devices are those deemed by the FDA to pose the greatest risk, such as life-sustaining, life supporting or implantable devices, or devices deemed not substantially equivalent to a previously 510(k) cleared device or a pre-amendment Class III device for which PMAs have not been called. Class III devices generally require PMA approval prior to marketing. The PMA approval pathway requires that the subject device demonstrates a reasonable assurance of the safety and effectiveness of the device.

A PMA for an IVD typically includes data from preclinical studies and well-controlled clinical trials. Preclinical data for an IVD includes many different tests, including how reproducible the results are when the same sample is tested multiple times by multiple users at multiple laboratories. The clinical data need to establish that the test is safe and effective for the proposed intended use in the indicated population. In addition, the PMA must include information regarding the test s clinical utility, meaning that an IVD provides information that is clinically meaningful. Such information must be provided even if the clinical significance of the biomarker is obvious. The applicant may also rely upon published literature or submit data to the FDA to show clinical utility.

A PMA also must provide information about the device and its components regarding, among other things, device design, manufacturing and labeling. The sponsor must pay an application fee to the FDA upon submission of a PMA, which is just under $250,000 for Fiscal Year 2017.

As part of the PMA review, the FDA will typically inspect the manufacturer s facilities for compliance with Quality System Regulation, or QSR, requirements, which impose elaborate testing, control, documentation and other quality assurance procedures.

Upon submission, the FDA determines if the PMA is sufficiently complete to permit a substantive review, and, if so, the FDA accepts the application for filing. The FDA then commences an in-depth review of the PMA. The entire process typically takes multiple years from submission of the PMA, but may take longer. The review time is often significantly extended as a result of the FDA asking for more information or clarification of information already provided. The FDA also may respond with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that are often expensive and time-consuming to generate and can substantially delay approval.

During the review period, an FDA advisory committee, typically a panel of clinicians, may be convened to review the PMA application and recommend to the FDA whether, or upon what conditions, the device should be approved. Although the FDA is not bound by the advisory panel decision, the panel s recommendation is important to the FDA s overall decision-making process.

If the FDA s evaluation of the PMA is favorable, the FDA typically issues an approvable letter requiring the applicant s agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA approval for the approved indications, which can be more limited than those

originally sought by the applicant. The PMA approval can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Failure to comply with the conditions of approval can result in an enforcement action, including the loss or withdrawal of the approval.

Even after approval of a PMA, a new PMA or PMA supplement may be required in the event of a modification to the device, its labeling or its manufacturing process. Supplements to a PMA often require the submission of the same type of information required for an original PMA, except that the supplement is generally limited to the information needed to support the proposed change from the product covered by the original PMA.

Clinical Trials and IDEs

A clinical trial is almost always required to support a PMA. For significant risk devices, the FDA regulations require that human clinical investigations conducted in the U.S. be approved via an Investigational Device Exemption, or IDE, which must be approved before clinical testing may commence. In some cases, one or more smaller IDE studies may precede a pivotal clinical trial intended to demonstrate the safety and efficacy of the investigational device. A 30-day waiting period after the submission of each IDE is required prior to the commencement of clinical testing in humans. FDA may disapprove, or approve with conditions, the IDE within the 30-day period. If disapproved, the clinical trial may not begin until the deficiencies noted by FDA are addressed, and another IDE is submitted to the FDA for approval. If approved with conditions, the sponsor must address the conditions prior to commencement of the trial. If FDA does not respond to the sponsor within the 30-day period, the IDE is deemed approved and the clinical study may commence.

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IVD trials usually do not require an IDE approval, so long as, among other things, the results of the IVD test are not used diagnostically without confirmation of the test results by another, medically established diagnostic product or procedure. For a trial where the IVD result directs the therapeutic care of patients with cancer, we believe that the FDA would likely consider the investigation to require an IDE application.

An IDE application must be supported by appropriate data, such as laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The IDE application must also include a description of product manufacturing and controls, and a proposed clinical trial protocol. The FDA typically grants IDE approval for a specified number of patients. All clinical studies of investigational devices, regardless of whether IDE approval is required, require approval from IRBs.

During the clinical trial, the sponsor must comply with the FDA s IDE requirements for investigator selection, trial monitoring, reporting and record keeping. The investigators must obtain patient informed consent, rigorously follow the investigational plan and study protocol, control the disposition of investigational devices and comply with all reporting and record keeping requirements. These IDE requirements apply to all investigational devices, whether considered significant or nonsignificant risk. Prior to granting PMA approval, the FDA typically inspects the records relating to the conduct of the study and the clinical data supporting the PMA for compliance with applicable requirements.

Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard intended to protect the rights and health of patients and to define the roles of clinical trial sponsors, investigators, and monitors; and (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. An IRB may also require the clinical trial at a study site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions.

Although the QSR does not fully apply to investigational devices, the requirement for controls on design and development does apply. The sponsor also must manufacture the investigational device in conformity with the quality controls described in the IDE application and any conditions of IDE approval that the FDA may impose with respect to manufacturing.

Investigational IVDs may only be distributed for use in an investigation, and the labeling must prominently contain the statement For Investigational Use Only. The performance characteristics of this product have not been established.

Expedited Access Pathway Program

In April 2015, the FDA issued a final guidance document establishing the EAP program. The EAP program is intended to speed patient access to devices (including companion diagnostics) that demonstrate the potential to address unmet medical needs for life threatening or irreversibly debilitating diseases or conditions and are subject to PMA approval or de novo authorization. In order to be accepted into the EAP program, a sponsor must demonstrate to the FDA s satisfaction that the device is intended to treat or diagnose a life-threatening or irreversibly debilitating disease or condition and that it addresses an unmet need. The sponsor must also submit an acceptable draft Data Development Plan. Once accepted into the program, the FDA intends to engage with sponsors of EAP Devices earlier and more interactively during the device s development, assessment, and review. The FDA will also work with the

device sponsor to try to reduce the time and cost from development to an approval decision. Elements of the EAP program may include priority review, interactive review, senior management involvement, and assignment of a case manager.

Post-Market Device Regulation

After a device obtains FDA approval and is on the market, numerous regulatory requirements apply. These requirements include the QSR, labeling regulations, the FDA s general prohibition against promoting products for unapproved or off-label uses, the Medical Device Reporting regulation, which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur, and the Reports of Corrections and Removals regulation, which requires manufacturers to report recalls and field actions to the FDA if initiated to reduce a risk to health posed by the device or to remedy a violation of the FDCA.

The FDA enforces these requirements by inspection and market surveillance. If the FDA finds a violation, it can institute a wide variety of enforcement actions, ranging from a public warning letter to more severe sanctions such as fines, injunctions and civil penalties; recall or seizure of products; operating restrictions, partial suspension or total shutdown of production; refusing requests for PMA approval of new products; withdrawing PMA approvals already granted; and criminal prosecution.

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Foreign Regulation

To obtain marketing approval of a drug under European Union regulatory systems, we may submit marketing authorization applications, or MAAs, either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The centralized procedure is compulsory for medicines produced by specified biotechnological processes, products designated as orphan medicinal products, and products with a new active substance indicated for the treatment of specified diseases, and optional for those products that are highly innovative or for which a centralized process is in the interest of patients. Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the Scientific Advice Working Party of the Committee of Medicinal Products for Human Use, or the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, defined by three cumulative criteria comprising the seriousness of the disease, such as heavy disabling or life-threatening diseases, to be treated; the absence or insufficiency of an appropriate alternative therapeutic approach; and anticipation of high therapeutic benefit. In this circumstance, the European Medicines Agency, or EMA, ensures that the opinion of the CHMP is given within 150 days.

The EMA grants orphan drug designation to promote the development of products that may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the European Union. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition in the European Union and without incentives it is unlikely that sales of the drug in the European Union would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the European Union of diagnosing, preventing or treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation provides opportunities for free protocol assistance, fee reductions for access to the centralized regulatory procedures before and during the first year after marketing authorization and between 6 and 10 years of market exclusivity following drug approval. The EMA has us granted orphan drug designation for entrectinib for the treatment of neuroblastoma.

The decentralized procedure for submitting an MAA provides an assessment of an application performed by one member state, known as the reference member state, and the approval of that assessment by one or more other member states, known as concerned member states. Under this procedure, an applicant submits an application, or dossier, and related materials, including a draft summary of product characteristics, and draft labeling and package leaflet, to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state s assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states. Prior to submitting an MAA for use of drugs in pediatric populations, the EMA requires submission of, or a request for waiver or deferral of, a Pediatric Investigation Plan.

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from assessing a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted but not approved for two years. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless

could also market another version of the drug if such company can complete a full MAA with a complete human clinical trial database and obtain marketing approval of its product.

Additional Regulations and Environmental Matters

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws restrict certain marketing practices in the pharmaceutical industry. These laws, which generally will not be applicable to us or our product candidates unless and until we obtain FDA marketing approval for any of our product candidates, include state and federal anti-kickback, fraud and abuse, false claims, physician payment sunshine and privacy and security laws and regulations regarding providing drug samples.

The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Violations of the federal anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, 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 federal False Claims Act.

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Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer.

The Health Insurance Portability and Accountability Act, or HIPAA, also created federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, 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. Similar to the federal anti-kickback statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA s security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys fees and costs associated with pursuing federal civil actions.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the Affordable Care Act, among other things, imposes reporting requirements on certain drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for knowing failures), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Drug manufacturers are required to submit reports to the government by the 90th day of each calendar year. Certain states also mandate implementation of compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of marketing expenditures and pricing information as well as gifts, compensation and other remuneration to physicians.

Additionally, the Prescription Drug Marketing Act, or the PDMA, imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations. If we obtain

approval from the FDA to market any of our drug product candidates, these product sampling restrictions may impact and curtail our marketing efforts to physicians.

Further, sales of any of our product candidates that may be approved will depend, in part, on the extent to which the cost of the product will be covered by third party payers. Third party payers may limit coverage to an approved list of products, or formulary, which might not include all drug products approved by the FDA for an indication. Any product candidates for which we obtain marketing approval may not be considered medically necessary or cost-effective by third party payers, and we may need to conduct expensive pharmacoeconomic studies in the future to demonstrate the medical necessity and/or cost effectiveness of any such product. The U.S. government, state legislatures and foreign governments have shown increased interest in implementing cost containment programs to limit government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Continued interest in and adoption of such controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals such as the product candidates we are developing.

Coverage and Reimbursement

Sales of any of our product candidates that may be approved will depend, in part, on the extent to which the cost of the product will be covered by third party payers. Third party payers may limit coverage to an approved list of products, or formulary, which might not include all drug products approved by the FDA for an indication. Any product candidates for which we obtain marketing approval may not be considered medically necessary or cost-effective by third party payers, and we may need to conduct expensive pharmacoeconomic studies in the future to demonstrate the medical necessity and/or cost effectiveness of any such product. The U.S.

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Healthcare Reform

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products, implementing reductions in Medicare and other healthcare funding, and applying new payment methodologies. For example, in March 2010, the Affordable Care Act was enacted, which, among other things, subjected drug manufacturers to new annual fees based on pharmaceutical companies share of sales to federal healthcare programs; created a new Patient Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; creation of the Independent Payment Advisory Board, which has authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs; and establishment of a Center for Medicare Innovation at the CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

We expect that the new presidential administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. Since taking office, President Trump has continued to support the repeal of all or portions of the Affordable Care Act. In January 2017, the House and Senate passed a budget resolution that authorizes congressional committees to draft legislation to repeal all or portions of the Affordable Care Act and permits such legislation to pass with a majority vote in the Senate. President Trump has also recently issued an executive order in which he stated that it is his administration s policy to seek the prompt repeal of the Affordable Care Act and directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the Affordable Care Act to the maximum extent permitted by law. There is still uncertainty with respect to the impact President Trump s administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the Affordable Care Act. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act to reduce healthcare expenditures. These changes include aggregate reductions of Medicare payments to providers of 2% per fiscal year that, due to subsequent legislative amendments, will remain in effect through 2025 unless additional action is taken by Congress. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, reform government program reimbursement methodologies.

Corporate Overview

Infinity Oil & Gas Company, or Parent, was incorporated under the laws of the State of Nevada on August 21, 2012. Ignyta was incorporated under the laws of the State of Delaware on August 29, 2011, with the name NexDx, Inc. On

October 31, 2013, IGAS Acquisition Corp, a wholly owned subsidiary of Parent, merged with and into Ignyta, and Ignyta survived the merger and became the wholly owned subsidiary of Parent. Upon the closing of the merger, Parent ceased to be a shell company under applicable rules of the U.S. Securities and Exchange Commission, or SEC. In connection with the merger, Parent changed its name to Ignyta, Inc. and Ignyta changed its name to Ignyta Operating, Inc.

On October 31, 2013, Parent effected a 100-to-one reverse stock split of its issued and outstanding shares of common stock, and all share information in this Annual Report on Form 10-K with respect to Parent gives retroactive effect to that reverse stock split.

On October 31, 2013, in connection with the closing of the merger, (i) all then-outstanding shares of each series of Ignyta s preferred stock were voluntarily converted into shares of Ignyta s common stock in accordance with Ignyta s certificate of incorporation, and (ii) Ignyta effected a three-to-one reverse stock split of its issued and outstanding shares of capital stock. All share information in this Annual Report on Form 10-K with respect to Ignyta s capital stock gives retroactive effect to that reverse stock split.

Concurrent with the closing of the merger, Parent abandoned its pre-merger business plan in the oil and gas industry, and we now solely pursue the business of Ignyta in the oncology drug development industry.

On June 12, 2014, Parent merged with and into Ignyta, with Ignyta surviving the merger and changing its name to Ignyta, Inc. The following discussion describes our current business.

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Employees

As of February 28, 2017, we had 112 employees, 108 of whom were full-time, including 34 employees with M.D. or Ph.D. degrees, and four part-time employees. Of these full-time and part-time employees, 80 employees were engaged in research and development activities. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Research and Development

Our research and development expenses for the years ended December 31, 2016, 2015 and 2014 were $76.9 million, $73.5 million, and $30.5 million, respectively.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We make available on our website at www.ignyta.com, free of charge, copies of these reports, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read or copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street NE, 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 an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov. The information in or accessible through the SEC s and our website are not incorporated into, and are not considered part of, this filing. Further, our references to the URLs for these websites are intended to be inactive textual references only.

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Item 1A. Risk Factors

We operate in a dynamic and rapidly changing environment that involves numerous risks and uncertainties. Certain factors may have a material adverse effect on our business, prospects, results of operations, financial condition and cash flows, and you should carefully consider them. Accordingly, in evaluating our business, we encourage you to consider the following discussion of risk factors, in its entirety, in addition to other information contained in this Annual Report on Form 10-K and our other public filings with the SEC. Other events that we do not currently anticipate or that we currently deem immaterial may also affect our business, prospects, financial condition and results of operations.

Risks Related to Our Financial Position and Capital Requirements

We have incurred significant losses since our inception and anticipate that we will continue to incur losses for the foreseeable future. We are a development-stage company with no approved products, and have generated no material revenue to date and may never generate material revenue or achieve profitability.

We are a development-stage biopharmaceutical company with a limited operating history. We have not generated any material revenue to date and are not profitable, and have incurred losses in each year since our inception. Our net loss for the year ended December 31, 2016 was $103.6 million. As of December 31, 2016, we had an accumulated deficit of $251.7 million. We expect to continue to incur losses for the foreseeable future, and we expect these losses to increase as we continue our development of, and seek regulatory approvals for, our product candidates, and begin to commercialize any approved products. We are currently focused on the development of our clinical and preclinical development programs, which we believe will result in our continued incurrence of significant research and development and other expenses related to those programs. If the non-clinical or clinical trials for any of our product candidates fail or produce unsuccessful results and those product candidates do not gain regulatory approval, or if any of our product candidates, if approved, fails to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders equity and working capital.

We expect to need additional funding to continue our operations, which could result in dilution or restrictions on our business activities. We may not be able to raise capital when needed, if at all, which would force us to delay, limit, reduce or terminate our product development programs or commercialization efforts and could cause our business to fail.

Our operations have consumed substantial amounts of cash since inception. We expect to need substantial additional funding to pursue our development programs and launch and commercialize any product candidates for which we receive regulatory approval, which may include building internal sales and marketing forces to address certain markets.

Even after giving effect to the proceeds received from our common stock offerings and our loan arrangement with SVB and Oxford, we expect to require substantial additional capital for the further development and commercialization of our product candidates. Further, we expect our expenses to increase in connection with our ongoing activities, particularly as we continue to expand our ongoing entrectinib and other development programs, and if we acquire rights to additional product candidates. For example, in September 2015 we initiated a new, global Phase 2 clinical trial of oral entrectinib in adult patients with advanced or metastatic cancer detected to be positive for relevant molecular alterations. We are conducting and plan to initiate additional clinical trials to study our other product candidates in the future.

In addition, if we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product manufacturing, marketing, sales and distribution. Furthermore, we expect to incur additional costs associated with our growth, as well as operating as a public company. For example, in October 2015 we signed a new lease for approximately 95,000 square feet of office and laboratory space, which lease became effective in the fourth quarter of 2016. We may also encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may increase our capital needs and/or cause us to spend our cash resources faster than we expect. Accordingly, we expect to need to obtain substantial additional funding in order to continue our operations.

To date, we have financed our operations entirely through equity investments and the incurrence of debt, and we expect to continue to do so in the foreseeable future. We may also seek funding through collaborative arrangements. Additional funding from those or other sources may not be available when or in the amounts needed, on acceptable terms, or at all. If we raise capital through the sale of equity, or securities convertible into equity, it would result in dilution to our then existing stockholders, which could be significant depending on the price at which we may be able to sell our securities. If we raise additional capital through the incurrence of further indebtedness, as we have done under our loan agreement with SVB and Oxford under which our ability to incur additional indebtedness is limited, we would likely become subject to additional covenants restricting our business activities, and holders of debt instruments may have rights and privileges senior to those of our equity investors. In addition, servicing the interest and principal

repayment obligations under debt facilities could divert funds that would otherwise be available to support research and development, clinical or commercialization activities. If we obtain capital through collaborative arrangements, these arrangements could require us to relinquish rights to our technology or product candidates and could result in our receipt of only a portion of the revenues associated with the partnered products. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, limit, reduce or terminate our research and development programs or any future commercialization efforts. Any of these events could significantly harm our business, financial condition and prospects.

We have incurred significant indebtedness under our loan agreement with SVB and Oxford, which will require substantial cash to service and which subjects our business to certain restrictions.

On June 30, 2016, we entered into a loan agreement with SVB as collateral agent and SVB and Oxford, collectively referred to as the Lenders, under which we incurred $32.0 million of indebtedness, substantially all of which was used to repay our then-existing $31.0 million loan with SVB. Under the loan agreement, we also have an option to receive an additional $10.0 million at any time from April 7, 2017 to August 31, 2017, provided that certain conditions have then been satisfied. We are required to pay interest on the borrowings under the loan agreement at a per-annum rate of Prime Rate plus 4.35% on a monthly basis for a period of 24 months. Thereafter, we will be required to repay the principal plus interest in 36 equal monthly installments; provided, however, that the interest-only period will be extended by an additional six months in the event we either (1) raise sufficient capital to trigger such extension under the terms of the loan agreement or (2) receive certain clinical trial data as required by the loan agreement. In the event that the interest only period is extended, the amortization period will be reduced to 30 months. Further, upon the maturity date the terms of the loan agreement require that we make a final lump-sum payment of 5% of the principal amount of the loans thereunder. We may elect to prepay all amounts owed under either or both of the loan tranches prior to the maturity date therefor, provided that a prepayment fee of 2% of the amount prepaid is also paid if the prepayment occurs on or prior to June 30, 2017, or 1% of amount prepaid is also paid, if the prepayment occurs thereafter.

Our ability to make scheduled payments on or to refinance our indebtedness depends on our future performance and ability to raise additional sources of cash, which is subject to economic, financial, competitive and other factors beyond our control. If we are unable to generate sufficient cash to service our debt, we may be required to adopt one or more alternatives, such as selling assets, restructuring our debt or obtaining additional equity capital on terms that may be onerous or highly dilutive. If we desire to refinance our indebtedness, our ability to do so will depend on the capital markets and our financial condition at such time.

We may not be able to engage in any of these activities or engage in these activities on desirable terms, which could result in a default on our debt obligations. Additionally, the loan agreement contains various covenants, including an obligation to deliver to the Lenders certain financial and insurance information and comply with certain notice requirements, and covenants that restrict our ability, without prior consent, to: incur certain additional indebtedness, enter into certain mergers, acquisitions or other business combination transactions, or incur any non-permitted lien or other encumbrance on our assets. Any failure by us to comply with any of those covenants, subject to certain cure periods, or to make all payments under the loan agreement when due, would cause us to be in default. In the event of any such default, the Lenders may be able to declare all borrowed funds, together with accrued and unpaid interest, immediately due and payable, thereby potentially causing all or substantial amounts of our available cash to be used to repay our indebtedness or forcing us into bankruptcy or liquidation if we do not then have sufficient cash available. Any such event or occurrence could severely and negatively impact our operations and prospects.

Our short operating history may hinder our ability to successfully meet our objectives, and may limit the amount of information about us upon which you can base an evaluation of our business and prospects.

The early stage nature of our business results in a limited operating history upon which you can evaluate our business and prospects. Our product candidates are at various stages of development, have not obtained regulatory marketing approval, have never generated any sales and require extensive testing before commercialization. Our limited operating history may adversely affect our ability to implement our business strategy and achieve our business goals, which include, among others, the following activities:

develop our product candidates;

obtain the human and financial resources necessary to develop, test, manufacture and market our product candidates;

continue to build and maintain an intellectual property portfolio covering our technology and our product candidates;

satisfy the requirements of clinical trial protocols, including patient enrollment, establish and demonstrate the clinical efficacy and safety of our product candidates and obtain necessary regulatory approvals;

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market our product candidates that receive regulatory approvals to achieve acceptance and use by the medical community in general;

develop and maintain successful collaboration, strategic and other relationships for the development and commercialization of our product candidates; and

manage our cash flows and any growth we may experience in an environment where costs and expenses relating to clinical trials, regulatory approvals and commercialization continue to increase. If we are unsuccessful in accomplishing these objectives, we may not be able to successfully develop product candidates, raise capital, expand our business or continue our operations.

Risks Related to Our Employees

If we are not able to attract and retain highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified personnel. We are highly dependent on our management, scientific and medical personnel, especially Jonathan E. Lim, M.D., our President, Chief Executive Officer and Chairman of the Board, whose services are critical to the successful implementation of our business strategies.

We are not aware of any present intention of any of our executive officers or other members of management to leave our company. However, our industry tends to experience a high rate of turnover of management personnel, and our personnel are generally able to terminate their relationships with us on short notice. All of our employment arrangements provide for at-will employment, which means that any of our employees could leave our employment at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior and mid-level managers as well as junior and mid-level scientific and medical personnel.

Moreover, there is intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses. Many of the other pharmaceutical companies against which we compete for qualified personnel have greater financial and other resources, different risk profiles, longer histories in the industry and greater ability to provide valuable cash or stock incentives to potential recruits 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 are able to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize product candidates will be limited.

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

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, through contractual provisions and other procedures, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee s former employers. Litigation may be

necessary to defend against any such claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact contributes to the development of intellectual property that we regard as our own. Further, the terms of such assignment agreements may be breached and we may not be able to successfully enforce their terms, which may force us to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of intellectual property rights we may regard and treat as our own.

Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could cause our business to suffer.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with regulations of governmental authorities, such as the FDA or the EMA, to provide accurate information to the FDA or EMA, to comply with manufacturing standards we have established, to comply with federal, state and international healthcare fraud

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and abuse laws and regulations, to report financial information or data accurately or to disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we currently take and the procedures we may establish in the future as our operations and employee base expand to detect and prevent this type of activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure by our employees to comply with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Related to the Development of Our Product Candidates

We are heavily dependent on the success of our current product candidates, which will require significant additional efforts to develop and may prove not to be viable for commercialization.

To date, we have invested significant efforts in the acquisition of our drug programs from NMS, Teva and Lilly. Our future success is substantially dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize products resulting from these programs and any others we may develop or acquire in the future, which may never occur.

Before we could generate any revenues from sales of our product candidates, we must complete the following activities for each of them, any one of which we may not be able to successfully complete:

- conduct substantial clinical development;
- manage clinical, preclinical and manufacturing activities;
- complete development of a proposed commercial formulation;
- achieve regulatory approvals;
- establish manufacturing relationships;
- build a commercial sales and marketing team, if we choose to market any such product ourselves, or enter into a collaboration to access sales and marketing functions;
- develop and implement marketing and reimbursement strategies;

develop and/or work with third-party collaborators to develop companion diagnostics and conduct clinical testing and achieve regulatory approvals for those companion diagnostics; and

invest significant additional cash in each of the above activities.

If the results of our ongoing or planned clinical trials of entrectinib and any other product candidates are not successful, we may not be able to use those results as the basis for advancing these product candidates into further clinical development. In that case, we may not have the resources to conduct new clinical trials, and/or we may determine that further clinical development of these product candidates is not justified and may decide to discontinue the programs. If the results of preclinical testing for our other product candidates are not successful, we may not be able to use those results as the basis for advancing those programs into further development. If studies of our product candidates produce unsuccessful results and we are forced or elect to cease their development, our business and prospects could be substantially harmed, particularly if the product candidates for which development has ceased are at the clinical development stage.

Preclinical and clinical testing of our product candidates that has been conducted to date may not have been performed in compliance with applicable regulatory standards, which could lead to increased costs or material delays for their further development.

We have only recently acquired the rights to develop our programs from NMS, Teva and Lilly, and the previous development of those programs was conducted wholly by such companies or any third parties with which they had contracted. As a result, we were not

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involved with nor did we have any control over any of those development activities. Because we had no input on those development activities, we may discover that all or certain elements of the trials and studies performed prior to our acquisition of rights to these programs have not been in compliance with applicable regulatory standards or have otherwise been deficient. If the previously conducted studies are not in full compliance with applicable regulatory standards or are otherwise not eligible for continued development in the United States or elsewhere, then we may be forced to conduct new studies in order to progress their development, which we may not have the funding or other resources to complete and which could severely delay any of our development plans for these product candidates. Any such deficiency in the prior development of these product candidates would significantly harm our business plans and prospects.

Our research and development efforts are based on a rapidly evolving area of science, and our approach to development is novel and may never lead to marketable products.

Biopharmaceutical product development is generally a highly speculative undertaking and by its nature involves a substantial degree of risk. Our specific line of business, the development of personalized drug therapeutics for patients with molecularly defined cancers, is an emerging field, and the scientific discoveries that form the basis for our efforts to develop product candidates are relatively new. Further, the scientific evidence to support the feasibility of developing product candidates based on those discoveries is both preliminary and limited. The failure of the scientific underpinnings of our business model to produce viable product candidates would substantially harm our operations and prospects.

We may not be successful in our efforts to build a pipeline of product candidates.

A key element of our strategy is to use and expand our product platform to build a pipeline of inhibitors of specific molecular targets, and progress those product candidates through clinical development for the treatment of a variety of different types of cancer. Although our research efforts to date have resulted in identification of a series of cancer drug targets, we may not be able to develop product candidates that are safe and effective inhibitors of any of these targets. Even if we are successful in building a product pipeline, the potential product candidates that we identify may not be suitable for clinical development for a number of reasons, including causing harmful side effects or demonstrating other characteristics that indicate a low likelihood of receiving marketing approval or achieving market acceptance. If our methods of identifying potential product candidates fail to produce a pipeline of potentially viable product candidates, then our success as a business will be dependent on the success of fewer potential product candidates, which introduces risks to our business model and potential limitations to any success we may achieve.

Clinical drug development involves a lengthy and expensive process with uncertain outcomes, and any of our clinical trials or studies could produce unsuccessful results or fail at any stage in the testing process.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Additionally, any positive results of preclinical studies and early clinical trials of a product candidate may not be predictive of the results of later-stage clinical trials, such that product candidates may reach later stages of clinical trials and fail to show the desired safety and efficacy traits despite having shown indications of those traits in earlier studies. For example, although the preclinical and early clinical results for our lead product candidate entrectinib have been promising, those results do not imply that later clinical trials will demonstrate similar results. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. The results of any future clinical trials we conduct may not be successful.

Although there are multiple clinical trials ongoing for entrectinib, RXDX-105 and taladegib we may experience delays in pursuing those or any other clinical or preclinical studies. Clinical trials can be delayed for a variety of reasons, including delays related to:

obtaining regulatory approval to commence a trial;

engaging leading clinical investigators and identifying sufficient clinical trial sites to conduct or support our clinical trials;

clinical protocol design and development, and reaching consensus with participating investigators on study design;

reaching agreement on acceptable contractual and financial terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;

obtaining approval from an independent institutional review board, or IRB, at each trial site;

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enrolling suitable patients to participate in a trial;

developing and validating companion diagnostics on a timely basis, and utilizing such companion diagnostics on an effective and timely basis;

changes in formulation, dosing or administration regimens;

having patients complete a trial or return for post-treatment follow-up;

clinical sites deviating from the trial protocol or dropping out of a trial;

regulators instituting a clinical hold due to observed safety findings;

changes in the regulatory, clinical or commercial landscape during the conduct of a trial that impair accrual;

findings from nonclinical toxicology or safety pharmacology studies or the requirement for such studies;

adding new clinical trial sites; or

manufacturing or having manufactured sufficient quantities of product candidate and the suitability of that product candidate for use in clinical trials on a timely basis.

We currently rely, and we expect to continue to rely, on CROs, clinical trial sites, contract manufacturers and other third parties to ensure the proper and timely conduct of our clinical trials. Although we have agreements in place with such third parties governing their committed activities and conduct, and we expect we will have similar agreements with other third parties we may engage in the future, we have limited influence over their actual performance. As a result, we ultimately do not have control over a third party s compliance with the terms of any agreement it may have with us, its compliance with applicable regulatory requirements, or its adherence to agreed time schedules and deadlines, and a third party s failure to perform those obligations could subject any of our clinical trials to delays or failure.

We could also encounter delays if a clinical trial is suspended or terminated by us, by the IRBs of the institutions in which such trials are being conducted, by the Data Monitoring Committee for the trial, if applicable, or by the FDA or other regulatory authorities. Such authorities may impose such a suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial sites by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we were to experience delays in the completion of, or suspension or termination of, any clinical trial for our product candidates, the commercial prospects of the product candidate would be harmed, and our

ability to generate product revenues from the product candidate would be delayed or eliminated. In addition, any delays in completing clinical trials would increase our costs, slow down our product candidate development and approval process and jeopardize regulatory approval of the product candidate. The occurrence of any of these events could harm our business, financial condition and prospects significantly.

If we experience delays or difficulties in the enrollment of patients in clinical trials, those clinical trials could take longer than expected to complete and our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our product candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. In particular, because we are primarily focused on patients with molecularly defined cancers which have relatively low incidence rates, our pool of suitable patients may be smaller and more selective and our ability to enroll a sufficient number of suitable patients may be limited or take longer than anticipated. For example, our product candidate entrectinib is designed as a targeted therapeutic candidate to treat patients with cancers that harbor activating alterations to *NTRK* (encoding TRK), *ROS1* (encoding ROS1) or *ALK* (encoding ALK). Our research to date indicates that *NTRK*, *ROS1* and *ALK* genes appear to be rearranged across a range of tumor types, with a frequency in the low single digit percentages, or possibly lower. The frequency at which *NTRK*, *ROS1* and *ALK* rearrangements are expressed in certain tumor types may affect our success in enrolling a suitable number of patients to participate in our clinical trials. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the

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same indications or target the same molecular alterations as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors product candidates.

Patient enrollment for any of our clinical trials may also be affected by other factors, including without limitation:

- the severity of the disease under investigation;
- the frequency of the molecular biomarker we are seeking to target in the applicable trial, and the ability to effectively identify such biomarker;
- the willingness of clinical sites and principal investigators to subject candidate patients to molecular screening;
- the eligibility criteria for the study in question;
- the perceived risks and benefits of the product candidate under study;
- the availability, effectiveness and safety of other treatment options;
- the extent of the efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of a sufficient number of clinical trial sites that are willing to comply with the requirements of our clinical protocols; and
- the presence of site-to-site variations at our clinical sites in the management of eligible study patients, which could impair our ability to interpret or generalize the results of the study. Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials would likely result in increased development costs for our product candidates, and we may not have or be able to obtain sufficient cash to fund such increased costs when needed, which could result in the further delay or termination of the trials.

Consistent with our general product development strategy, we designed our ongoing Phase 2 clinical trial of entrectinib, and we generally expect to design any other trials for that and our other product candidates, to include

patients with applicable molecular alterations or biomarkers, with a view to assessing possible early evidence of potential therapeutic effect. If we are unable to locate and include such patients in those trials, then our ability to make those early assessments and to seek participation in FDA expedited review and approval programs, including accelerated approval, breakthrough therapy and fast track designation, or otherwise to seek to accelerate clinical development and regulatory timelines, could be compromised.

The approval processes of regulatory authorities are lengthy, time consuming, expensive and inherently unpredictable. If we are unable to obtain approval for our product candidates from applicable regulatory authorities, we will not be able to market and sell those product candidates in those countries or regions and our business will be substantially harmed.

The time required to obtain approval by the FDA, EMA and comparable foreign authorities is unpredictable, but typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of the regulatory authorities. We have not submitted an NDA or similar filing or obtained regulatory approval for any product candidate in any jurisdiction and it is possible that none of our existing product candidates or any product candidates we may seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including any one or more of the following:

- the FDA, EMA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;

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- we may be unable to demonstrate to the satisfaction of the FDA, EMA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;

- the results of clinical trials may not meet the level of statistical significance required by the FDA, EMA or comparable foreign regulatory authorities for approval;

- we may be unable to demonstrate that a product candidate s clinical and other benefits outweigh its safety risks;

- the FDA, EMA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

- the data collected from clinical trials of our product candidates may not be sufficient to support the submission of an NDA or other submission or to obtain regulatory approval in the United States or elsewhere;

- the FDA, EMA or comparable foreign regulatory authorities may fail to hold to previous agreements or commitments;

- the FDA, EMA or comparable foreign regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with which we contract for clinical and commercial supplies;

- the FDA, EMA or comparable foreign regulatory authorities may fail to approve the companion diagnostics we contemplate developing internally or with partners; and

- the approval policies or regulations of the FDA, EMA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

The time and expense of the approval process, as well as the unpredictability of future clinical trial results and other contributing factors, may result in our failure to obtain regulatory approval to market, in one or more jurisdictions, entrectinib or any other product candidate, which would significantly harm our business, results of operations and prospects.

In order to market and sell our products in any jurisdiction, we or our third party collaborators must obtain separate marketing approvals in that jurisdiction and comply with its regulatory requirements. The approval procedure can vary drastically among countries, and each jurisdiction may impose different testing and other requirements to obtain and maintain marketing approval. Further, the time required to obtain those approvals may differ substantially among jurisdictions. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. Moreover, approval by the FDA or an equivalent foreign authority does not ensure approval by regulatory authorities in any other countries or jurisdictions.

As a result, the ability to market and sell a product candidate in more than one jurisdiction can involve significant additional time, expense and effort to undertake separate approval processes, and could subject us and our collaborators to the numerous and varying post-approval requirements of each jurisdiction governing commercial sales, manufacturing, pricing and distribution of our product candidates. We or any third parties with whom we may collaborate may not have the resources to pursue those approvals, and we or they may not be able to obtain any approvals that are pursued. The failure to obtain marketing approval for our product candidates in foreign jurisdictions could severely limit their potential markets and our ability to generate revenue.

In addition, even if we were to obtain regulatory approval in one or more jurisdictions, regulatory authorities may approve any of our product candidates for fewer or more limited indications than we request, may not approve the prices we may propose to charge for our products, may grant approval contingent on the performance of costly post-marketing clinical trials, or may approve a product candidate with labeling that does not include the claims necessary or desirable for the successful commercialization of that product candidate. Any of the foregoing circumstances could materially harm the commercial prospects for our product candidates.

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

To date, patients treated with entrectinib, RXDX-105 and taladegib have experienced some AEs that are deemed to be drug related. Results of our ongoing or future clinical trials of these or our other product candidates could reveal a high and/or unacceptable severity and frequency of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of, or deny approval of, our product candidates for any or all targeted indications. Further, any observed drug-related side effects could affect patient recruitment or the ability of

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enrolled patients to complete the trial, or result in potential product liability claims. Any of these occurrences could materially harm our business, financial condition and prospects.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings in the product s labeling;
- we may be required to create a medication guide for distribution to patients that outlines the risks of such side effects;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product, if approved, and could significantly harm our business, results of operations and prospects.

Failure to successfully validate, develop and obtain regulatory approval for companion diagnostics could harm our drug development strategy and operational results.

As one of the central elements of our business strategy and clinical development approach, we seek to identify molecularly-defined subsets of patients within a disease category who may derive selective and meaningful benefit from the product candidates we are developing. In order to assist in identifying those subsets of patients, a companion diagnostic, which is a test or measurement that evaluates the presence of biomarkers in a patient, could be used. We anticipate that the development of companion diagnostics concurrently with some of our product candidates will help us more accurately identify the patients who belong to the target subset, both during our clinical trials and in connection with the commercialization of product candidates. In June 2015, we announced the release for clinical use of our first clinical trial assay to support patient identification and enrollment into our Phase 2 clinical trial of entrectinib, but we have not developed or offered any companion diagnostics for commercial use. We may need to rely on third party collaborators to successfully develop and commercialize companion diagnostics. To date, we have not developed relationships with any such third-party collaborators to develop companion diagnostics for any of our product candidates.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and require separate regulatory clearance or approval prior to their commercialization. We may be dependent on the sustained cooperation and effort of any third-party collaborators with whom we may partner in the future to develop and obtain clearance or approval for these companion diagnostics, and we may not be able to establish arrangements with any such third-party collaborators for the development and production of companion diagnostics when needed or on terms that are beneficial to us, or at all. We and our potential future collaborators may encounter

difficulties in developing and obtaining approval for these companion diagnostics, including issues relating to the selectivity and/or specificity of the diagnostic, analytical validation, reproducibility, or clinical validation. In November 2016, the FDA granted our request to review the Trailblaze Pharos companion diagnostic test service under the EAP program because it met the three criteria necessary for inclusion in the program, one of which is addressing an unmet clinical need. Once accepted into the EAP program, the FDA will work with the device sponsor to try to reduce the time and cost from development to an approval decision. Acceptance into the EAP program does not guarantee that a product will be developed or reviewed more quickly, nor does it guarantee approval of the PMA for Trailblaze Pharos by the FDA. Since FDA generally requires concurrent approval of a companion diagnostic and therapeutic product, any delay or failure by us or our potential future collaborators to develop or obtain regulatory clearance or approval of any companion diagnostics could delay or prevent approval of our related product candidates. In addition, our potential future collaborators may encounter production difficulties that could constrain the supply of the companion diagnostics, and we or they may experience difficulties gaining acceptance of the use of the companion diagnostics in the clinical community. In addition, any third parties with whom we may contract to develop and produce companion diagnostics could decide to discontinue selling or manufacturing the companion diagnostic, and we may not be able to enter into arrangements with other parties to obtain supplies of alternative diagnostic tests on a timely basis or reasonable terms, or at all. The occurrence of any such event could adversely affect and/or delay the development or commercialization of our product candidates.

We may expend our limited resources to pursue a particular product candidate or indication that does not produce any commercially viable products and may fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

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Because we have limited financial and managerial resources, we must focus our efforts on particular product candidates for specific indications. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Further, our resource allocation decisions may result in our use of funds for research and development programs and product candidates for specific indications that may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Any such failure to properly assess potential product candidates could result in missed opportunities and/or our focus on product candidates with low market potential, which would harm our business and financial condition.

We may not be able to obtain orphan drug exclusivity for the product candidates for all indications for which we seek or receive regulatory approval, which could limit the potential profitability of such product candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States. Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it receives the designation, then the product is entitled to a period of marketing exclusivity that precludes the applicable regulatory authority from approving another marketing application for the same drug for the exclusivity period for the same indication, except in limited situations.

The FDA and the EMA have granted us orphan drug designation for entrectinib for the treatment of neuroblastoma, and the FDA has granted us orphan drug designation for entrectinib for the treatment of TRKA-positive, TRKB-positive, TRKC-positive, ROS1-positive or ALK-positive non-small cell lung cancer and colorectal cancer. We expect that we may in the future pursue orphan drug designations for entrectinib in other jurisdictions and/or indications, and for at least some of our other product candidates. Obtaining orphan drug designations can be difficult and we may not be successful in doing so. In addition, orphan drug exclusivity may not effectively protect a product from the competition of different drugs for the same indication, which could be approved during the exclusivity period. Further, after an orphan designated drug is approved and if it obtains orphan drug exclusivity, the FDA could subsequently approve another application for the same drug for the same indication if the FDA concludes that the later drug is shown to be safer, more effective or makes a major contribution to patient care. The failure to obtain an orphan drug designation for any product candidates for rare cancer indications for which we seek or receive regulatory approval, and/or the inability to maintain that designation for the duration of the applicable exclusivity period, could reduce our ability to make sufficient sales of the applicable product candidate to balance our expenses incurred to develop it, which would have a negative impact on our operational results and financial condition.

Our product candidates are in various stages of development and may never be fully developed in a manner suitable for commercialization. If we do not develop commercially successful products, our ability to generate revenue will be limited.

We currently have no products that are approved for commercial sale. All of our product candidates are in various stages of development, and significant research and development, financial resources and personnel will be required to develop commercially viable products and obtain regulatory approvals. Further, certain of the indications that we are pursuing have relatively low incidence rates, which may make it difficult for us to enroll a sufficient number of patients in our clinical trials on a timely basis, or at all, and may limit the revenue potential of our product candidates. If we are unable to develop, receive approval for, or successfully commercialize any of our product candidates, we

may be unable to generate meaningful revenue from product sales and will incur continued net losses and negative cash flows.

If we seek and obtain a fast track or breakthrough therapy designation or accelerated approval by the FDA for any of our product candidates, such designations may not actually lead to a faster development or regulatory review or approval process or any other material benefits.

We may in the future seek fast track designation for some of our product candidates that reach the regulatory review process. If a product candidate is intended for the treatment of a serious or life-threatening condition and the product candidate demonstrates the potential to address unmet medical needs for this condition, the sponsor may apply to the FDA for a fast track designation for the product candidate. If fast track designation is obtained, the FDA may initiate review of sections of an NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the remaining information. In addition, a fast track product may be eligible for accelerated approval, as described below. The FDA has broad discretion over whether to grant a fast track designation and, as a result, even our product candidates that may be eligible for such a designation may not receive it. Even if we were to receive fast track designation for any of our product candidates, the designation may not result in a

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materially faster development process, review or approval compared to conventional FDA procedures. Additionally, the FDA could withdraw a fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

Additionally, we may in the future seek a breakthrough therapy designation for our product candidates. The Food and Drug Administration Safety and Innovation Act established the breakthrough therapy designation for drugs intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and that, as indicated by preliminary clinical evidence, may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies by the FDA are eligible for accelerated approval and increased interaction and communication with the FDA designed to expedite the development and review process.

As with fast track designation, designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and may determine not to grant such a designation. Even if we receive a breakthrough therapy designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional FDA procedures. Further, obtaining a breakthrough therapy designation does not assure or increase the likelihood of the FDA s approval of the applicable product candidate. In addition, even if one or more of our product candidates qualifies as a breakthrough therapy, the FDA could later determine that those products no longer meet the conditions for the designation or determine not to shorten the time period for FDA review or approval.

We may also in the future seek accelerated approval for some of our product candidates. Under the FDA s accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening disease or condition that provides meaningful therapeutic benefit to patients over existing treatments and demonstrates an effect based upon 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. In clinical trials, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or sooner than clinical endpoints. As with fast track designation and breakthrough therapy designation, the FDA has broad discretion over whether to grant approval based on a surrogate endpoint. Accordingly, even if we believe one of our product candidates meets the criteria for accelerated approval, the FDA may disagree and may determine not to grant such approval.

In addition, a product candidate approved on such an accelerated basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to validate the surrogate endpoint or otherwise confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis.

The FDA has granted rare pediatric disease designation to entrectinib for the treatment of neuroblastoma; however, an NDA for entrectinib, if approved, may not meet the eligibility criteria for a priority review voucher.

The FDA has granted rare pediatric disease designation to entrectinib for the treatment of neuroblastoma. Designation of a drug as a drug for a rare pediatric disease does not guarantee that an NDA for such drug will meet the eligibility criteria for a rare pediatric disease priority review voucher at the time the application is approved. Under the FDCA, we will need to request a rare pediatric disease priority review voucher in our original NDA for entrectinib. The FDA

may determine that an NDA for entrectinib, if approved, does not meet the eligibility criteria for a priority review voucher, including for the following reasons:

- neuroblastoma no longer meets the definition of a rare pediatric disease;
- the NDA contains an active ingredient (including any ester or salt of the active ingredient) that has been previously approved in an NDA;
- the NDA is not deemed eligible for priority review;
- the NDA does not rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population (that is, if the NDA does not contain sufficient clinical data to allow for adequate labeling for use by the full range of affected pediatric patients); or

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the NDA is approved for a different adult indication than the rare pediatric disease for which entrectinib is designated (for example, if entrectinib is approved for an indication based on specific genetic alterations that would be inclusive of but not limited to neuroblastoma).

The authority for the FDA to award rare pediatric disease priority review vouchers for drugs that have received rare pediatric disease designation prior to September 30, 2020 currently expires on September 30, 2022. If the NDA for entrectinib is not approved prior to September 30, 2022 for any reason, regardless of whether it meets the criteria for a rare pediatric disease priority review voucher, it will not be eligible for a priority review voucher. However, it is also possible the authority for FDA to award rare pediatric disease priority review vouchers will be further extended through Federal lawmaking.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct preclinical and clinical trials of our product candidates. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We rely, and expect to continue to rely, upon third-party CROs to execute our preclinical and clinical trials and to monitor and manage data produced by and relating to those trials. However, we may not be able to establish arrangements with CROs when needed or on terms that are acceptable to us, or at all, which could negatively affect our development efforts with respect to our drug product candidates and materially harm our business, operations and prospects.

We currently have only limited control over the activities of the CROs we have engaged to continue the ongoing and planned clinical trials for entrectinib, RXDX-105 and taladegib, and we expect the same to be true for any CROs we may engage in the future. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on any CRO does not relieve us of our regulatory responsibilities. Based on our present expectations, we, our CROs and our clinical trial sites are required to comply with good clinical practices, or GCPs, for all of our product candidates in clinical development. Regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in the applicable trial may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require us to perform additional clinical trials before approving a product candidate for marketing, which we may not have sufficient cash or other resources to support and which would delay our ability to generate revenue from any sales of such product candidate. In addition, our clinical trials are required to be conducted with product produced in compliance with current good manufacturing practice requirements, or cGMPs. Our or our CROs failure to comply with those regulations may require us to repeat clinical trials, which would also require significant cash expenditures and delay the regulatory approval process.

Agreements governing relationships with CROs generally provide those CROs with certain rights to terminate the agreements under specified circumstances. If a CRO that we have engaged terminates its relationship with us during the performance of a clinical trial, we would be forced to seek an engagement with a substitute CRO, which we may not be able to do on a timely basis or on commercially reasonable terms, if at all, and the applicable trial would experience delays or may not be completed and would likely increase in cost. In addition, our CROs are not our employees, and except for remedies available to us under any agreements we enter with them, we are unable to control whether or not they devote sufficient time and resources to our clinical and preclinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to a failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and

we may not be able to obtain regulatory approval for, or successfully commercialize, the affected product candidates. As a result, our operations and the commercial prospects for the affected product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

We plan to rely solely on third parties to manufacture our preclinical and clinical drug supplies and any approved product candidates, and our operations could be harmed if those third parties fail to provide sufficient quantities of product in accordance with applicable regulatory and contractual obligations or if we are otherwise unable to secure sufficient quantities.

We do not currently have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our preclinical and clinical drug supplies for use in the conduct of our preclinical studies and clinical trials or commercial quantities of any product candidates that may obtain regulatory approval. As a result, we expect that we will need to rely solely on third-party manufacturers for those services. We have a limited number of supply arrangements for entrectinib, and we are currently reliant on a single contract manufacturer for the clinical supply of RXDX-105. In addition, we have only a limited clinical supply of taladegib, and we must seek to establish clinical supply agreements with third parties for future supplies. We do not currently have arrangements in place for commercial supply of bulk drug substance or drug products. We may not be able to establish these or any other supply relationship

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when needed, on reasonable terms, or at all, in particular given the limited number of qualified third-party manufacturers and existing limitations on their production capacity. Any failure to secure sufficient supply of our product candidates for preclinical or clinical testing or, in the future, commercial purposes would materially harm our operations and financial results.

We expect that the facilities to be used by any contract manufacturers we engage to manufacture our product candidates will be inspected by the FDA in connection with any NDA that we submit. We do not control the manufacturing process of, and are and will continue to be dependent on, our contract manufacturing partners for compliance with cGMPs for the manufacture of clinical and, if regulatory approval is obtained, commercial quantities of our product candidates. If any of our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or other comparable foreign authorities, we would be prevented from obtaining regulatory approval for our product candidates or commercializing our products, if approved, unless and until we could engage a substitute contract manufacturer that could comply with such requirements, which we may not be able to do. In recent years, the FDA has issued complete response letters and declined to approve marketing applications submitted by various companies due to adverse findings at the contract manufacturers facilities that were identified in connection with pre-approval or other inspections at these facilities. Any such failure by any of our contract manufacturers would significantly impact our ability to continue to develop, obtain regulatory approval for or market our product candidates, if approved.

We expect to rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our preclinical studies and clinical trials or for commercial sale. We do not have, nor do we expect to enter, any agreements for the production of these raw materials, and we do not expect to have any control over the process or timing of our manufacturers acquisition of raw materials needed to produce our product candidates. Any significant delay in the supply of a product candidate or the raw material components thereof for an ongoing preclinical study or clinical trial due to a manufacturer s need to replace a third-party supplier of raw materials could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our product candidates. Additionally, if our manufacturers or we are unable to purchase these raw materials to commercially produce any of our product candidates that gain regulatory approval, the commercial launch of our product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenues from the sale of our product candidates.

Risks Related to Any Commercialization of Our Product Candidates

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and review. Maintaining compliance with ongoing regulatory requirements may result in significant additional expense to us, and any failure to maintain such compliance could subject us to penalties and cause our business to suffer.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product. In addition, if the FDA, EMA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, AE reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, as well as continued compliance with cGMPs and cGCPs for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including AEs of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

restrictions on the marketing or manufacturing of the product, product recalls or complete withdrawal of the product from the market;

fines, warning or untitled letters or holds on post-approval clinical trials;

refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;

product seizure or detention, or refusal to permit the import or export of products; and

consent decrees, injunctions or the imposition of civil or criminal penalties.

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The FDA s or EMA s policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs, biologics, and devices and to spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are otherwise not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

In addition, we also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA s ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, on January 23, 2017, President Trump ordered a hiring freeze for all executive departments and agencies, including the FDA, which prohibits the FDA from filling employee vacancies or creating new positions. Under the terms of the order, the freeze will remain in effect until implementation of a plan to be recommended by the Director for the Office of Management and Budget, or OMB, in consultation with the Director of the Office of Personnel Management, to reduce the size of the federal workforce through attrition. Although certain positions at the FDA may be exempt from the freeze, an under-staffed FDA could result in delays in FDA s responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the two-for-one provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the two-for-one provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA s ability to exercise its regulatory authority. If these executive actions impose constraints on FDA s ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

We currently have limited marketing personnel and no sales force. If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, we may not be able to effectively market and sell our product candidates, if approved, or generate product revenues.

We currently have limited marketing personnel and no sales team for the marketing, sales and distribution of any of our product candidates that are able to obtain regulatory approval. In order to commercialize any product candidates, we must build on a territory-by-territory basis marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. If we further develop these capabilities internally, the process will be expensive and time consuming and will require significant attention of our executive officers to manage. If we choose to collaborate, either globally or on a territory-by-territory basis, with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems, we

may be unable to enter into such arrangements when needed on acceptable terms or at all and we are likely to have limited control over the efforts of our collaborators. If we are not successful in commercializing our product candidates, either on our own or through collaborations with one or more third parties, our future product revenue will suffer and we may incur significant additional losses.

Our commercial success depends upon attaining significant market acceptance of our product candidates, if approved, among physicians, patients, healthcare payers and operators of major cancer clinics.

Even if we obtain regulatory approval for our product candidates, the products may not gain market acceptance among physicians, health care payers, patients and the medical community, which is critical to commercial success. Market acceptance of any product candidate for which we receive approval depends on a number of factors, including:

the efficacy and safety as demonstrated in clinical trials;

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the timing of market introduction of the product candidate, any associated companion diagnostic, and/or competitive products;

the clinical indications for which the drug is approved;

the approval, availability, market acceptance and reimbursement for any companion diagnostic;

the ability of a companion diagnostic to successfully identify all tested patients that harbor the underlying molecular biomarker that our product targets;

acceptance of the drug as a safe and effective treatment by physicians, operators of major cancer clinics and patients;

the size of the markets for the product candidate, based on the size of the patient subsets that we are targeting, in the territories for which we gain regulatory approval and have commercial rights;

the potential and perceived advantages of the product candidate over alternative treatments, especially with respect to patient subsets that we are targeting with the product candidate;

the safety of the product candidate as demonstrated through broad commercial use including, potentially, under conditions not tested in clinical trials;

the cost of treatment in relation to alternative treatments;

the availability of adequate reimbursement and pricing by third-party payers and government authorities;

relative convenience and ease of administration;

the prevalence and severity of adverse side effects; and

the effectiveness of our sales, marketing and distribution efforts.

If our product candidates are approved but fail to achieve an adequate level of acceptance by key market participants, we will not be able to generate significant revenues, and we may not become or remain profitable.

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

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. In addition, competition in the oncology market is intense. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions.

With respect to entrectinib, we are aware that Loxo Oncology is developing larotrectnib (LOXO-101) for patients with TRK-positive solid tumors, and has initiated a Phase 2 basket trial in adult cancer patients whose tumors harbor TRK fusions and a Phase 1/1b trial in pediatric cancer patients. We are also aware of three agents that have been approved by the FDA for ALK-positive NSCLC Pfizer s Xalkori®/crizotinib, Novartis Zykadia®/ceritinib and Roche s Alecensa®/alectinib. Alectinib is also approved for this indication in Japan. In addition, we are aware that Pfizer s Xalkori®/crizotinib has also been approved by the FDA for ROS1-positive NSCLC.

With respect to taladegib, we are aware of two agents that have been approved by the FDA to treat basal cell carcinoma and are designed to selectively inhibit the hedgehog pathway by binding the smoothened protein: Genentech s Erivedge®/vismodegib and Novartis Odomzo®/sonidegib.

We are also aware of several other products in development targeting TRKA, TRKB, TRKC, ROS1, ALK, Hedgehog/Smoothened, RET, TYRO3, AXL, MER, and/or c-MET for the treatment of cancer, some of which may be in a more advanced stage of development than our product candidates. There are also many other compounds directed to other molecular targets that are in clinical development by a variety of companies to treat cancer types that we may choose to pursue with our programs.

Many of our competitors have substantially greater financial, technical and other resources than we do, such as larger research and development staff and experienced marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and

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pharmaceutical industries may result in even more resources being concentrated in certain of our competitors. As a result of these or other factors, these companies may be able to obtain regulatory approval more rapidly than we can and may be more effective in selling and marketing their products. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing drug products that are more effective or less costly to produce or purchase on the market than any product candidate we are currently developing or that we may seek to develop in the future. If approved, our product candidates will face competition from commercially available drugs as well as drugs that are in the development pipelines of our competitors.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of or in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Our competitors may succeed in obtaining patent protection, receiving FDA, EMA or other regulatory approvals, or discovering, developing and commercializing medicines before we do, which would have a material adverse impact on our business and ability to achieve profitability from future sales of our approved product candidates, if any.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell on a profitable basis any product candidates for which we obtain marketing approvals.

There is significant uncertainty related to the third-party coverage and reimbursement of newly approved drugs and companion diagnostics. Market acceptance and sales of any of our product candidates that obtain regulatory approval in domestic or international markets will depend significantly on the availability of adequate coverage and reimbursement from third-party payers and may be affected by existing and future healthcare reform measures.

Pricing and reimbursement for any of our approved product candidates is uncertain. Government authorities and other third-party payers decide which drugs and laboratory tests they will pay for and establish reimbursement levels for them, and obtaining coverage and reimbursement approval for a product from any such third-party payer is a time consuming and costly process. Adoption of our product candidates by the medical community may be limited if doctors, patients and other key market participants do not receive adequate partial or full reimbursement for our approved products. As a result, any denial of private or government payer coverage or inadequate reimbursement for use of our approved product candidates could harm our business and diminish our prospects for generating revenue.

In some foreign countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can be a long and expensive process after the receipt of marketing approval for a product candidate. To obtain reimbursement or pricing approval in some countries, we may be required to conduct additional clinical trials that compare the cost-effectiveness of our product candidates to other available therapies. If reimbursement of our product candidates is unavailable or limited in scope or amount in a particular country, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability for sales of any of our product candidates that are approved for marketing in that country.

Healthcare legislative reform measures may have a material adverse effect on our business and results of operations.

There have been, and may continue to be, legislative and regulatory proposals at the federal and state levels and in foreign jurisdictions directed at broadening the availability and containing or lowering the cost of healthcare. The continuing efforts of the government, insurance companies, managed care organizations and other payers to contain or reduce costs of healthcare may adversely affect our ability to set prices for our products that would allow us to achieve or sustain profitability. In addition, governments may impose price controls on any of our product candidates that obtain marketing approval, which may adversely affect our future profitability.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or the Affordable Care Act, was passed, which substantially changed the way health care is financed by both governmental and private insurers, and significantly impacted the U.S. pharmaceutical industry. The Affordable Care Act, among other things, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer

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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.

We expect that the new presidential administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the Affordable Care Act. Since taking office, President Trump has continued to support the repeal of all or portions of the Affordable Care Act. In January 2017, the House and Senate passed a budget resolution that authorizes congressional committees to draft legislation to repeal all or portions of the Affordable Care Act and permits such legislation to pass with a majority vote in the Senate. President Trump has also recently issued an executive order in which he stated that it is his administration s policy to seek the prompt repeal of the Affordable Care Act and directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the Affordable Care Act to the maximum extent permitted by law. There is still uncertainty with respect to the impact President Trump s administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the Affordable Care Act. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, other legislative changes have been proposed and adopted in the United States since the Affordable Care Act was enacted. These changes include aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Recently there has also been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products.

Moreover, payment methodologies, including payment for companion diagnostics, may be subject to changes in healthcare legislation and regulatory initiatives. For example, CMS began bundling the Medicare payments for certain laboratory tests ordered while a patient received services in a hospital outpatient setting. Additionally, on April 1, 2014, the Protecting Access to Medicare Act of 2014, or PAMA, was signed into law, which, among other things, significantly alters the current payment methodology under the CLFS. Under the new law, starting January 1, 2017 and every three years thereafter (or annually in the case of advanced diagnostic lab tests), clinical laboratories must report laboratory test payment data for each Medicare-covered clinical diagnostic lab test that it furnishes during a time period to be defined by future regulations. The reported data must include the payment rate (reflecting all discounts, rebates, coupons and other price concessions) and the volume of each test that was paid by each private payer (including health insurance issuers, group health plans, Medicare Advantage plans and Medicaid managed care organizations). Beginning in 2018, the Medicare payment rate for each clinical diagnostic lab test, with some exceptions, will be equal to the weighted median private payer payment for the test, as calculated using data collected by applicable laboratories during the data collection period and reported to CMS during a specified data reporting period. Also under PAMA, CMS is required to adopt temporary billing codes to identify new clinical diagnostic laboratory tests and advanced diagnostic laboratory tests that do not already have unique diagnostic codes, and that have been cleared or approved by the FDA.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could

result in reduced demand for our drug candidates or companion diagnostics or additional pricing pressures.

We could be subject to product liability lawsuits based on the use of our product candidates in clinical testing or, if obtained, following marketing approval and commercialization. If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to cease clinical testing or limit commercialization of our product candidates.

We could be subject to product liability lawsuits if any product candidate we develop allegedly causes injury or is found to be otherwise unsuitable for human use during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability, breach of warranties or other claims. Claims could also be asserted under state consumer protection acts or other laws. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit clinical testing of our product candidates or commercialization, if approved. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

decreased demand for our product candidates;

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injury to our reputation;

withdrawal of clinical trial participants;

initiation of investigations by regulators;

costs to defend the related litigation;

a diversion of management s time and our resources;

substantial monetary awards to trial participants or patients;

product recalls, withdrawals or labeling, marketing or promotional restrictions;

loss of revenues from product sales; and

the inability to commercialize our product candidates.

Our inability to retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the clinical testing and commercialization of products we develop. We have obtained product liability insurance covering our clinical trials of entrectinib, RXDX-105 and taladegib, as well as our terminated clinical trial of RXDX-107. We may wish to obtain additional such insurance should we seek to expand those clinical trials or commence new clinical trials. We also may determine that additional types and amounts of coverage would be desirable at later stages of clinical development of our product candidates or upon commencing commercialization of any product candidate that obtains required approvals. However, we may not be able to obtain any such additional insurance coverage when needed on acceptable terms, or at all. We could be responsible for some or all of the financial costs associated with a product liability claim relating to our development or commercialization activities, in the event that any such claim results in a court judgment or settlement in an amount or of a type that is not covered, in whole or in part, by any insurance policies we may have or that is in excess of the limits of our insurance coverage. We may not have, or be able to obtain, sufficient capital to pay any such amounts that may not be covered by our insurance policies.

Risks Related to Our Intellectual Property

If we breach any of the agreements under which we license from third parties the development and commercialization rights to our product candidates, we could lose license rights that are important to our business and our operations could be materially harmed.

We have in-licensed from NMS the use, development and commercialization rights for our entrectinib program. We have in-licensed from Lilly the use, development and commercialization rights for our taladegib programs, and we have assumed license agreements from Teva that include rights and obligations relating to our RXDX-105 and

RXDX-106 programs. As a result, our current business plans are dependent upon our satisfaction of certain conditions to the maintenance of those license agreements and the rights we license under them. Each of the license agreements provides that we are subject to diligence obligations relating to the commercialization and development of product candidates, milestone payments, royalty payments and other obligations. In addition to these license agreements, we may seek to enter into additional agreements with other third parties in the future granting similar license rights with respect to other potential product candidates. If we fail to comply with any of the conditions or obligations or otherwise breach the terms of any of these license agreements, or any future license agreement we may enter on which our business or product candidates are dependent, the licensor may have the right to assert a claim for damages against us or terminate the applicable agreement in whole or in part and thereby extinguish our rights to the licensed technology and intellectual property and/or any rights we have acquired to develop and commercialize certain product candidates. If we become liable for material damages under any of these license agreements, this could materially harm our business, prospects, financial condition and results of operations. Similarly, the loss of the rights licensed to us under these license agreements, or any future license agreement that we may enter granting us rights on which our business or product candidates are dependent, would eliminate our ability to further develop the applicable product candidates and would materially harm our business, prospects, financial condition and results of operations.

If our efforts to protect the proprietary nature of the intellectual property related to our technologies are not adequate, we may not be able to compete effectively in our markets and our business would be harmed.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies. The breadth, validity and enforceability of patents in the biotechnology and pharmaceutical field involves

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complex legal and scientific questions and can be uncertain. The standards of patentability and patent eligibility for diagnostic methods, personalized medicine, and biotechnology inventions are evolving and to some extent uncertain, and subject matter that is presently considered to be patentable may not be patentable (and patents directed thereto might not be valid) in the future. It is possible that we will fail to identify patentable aspects of our development activities before it is too late to obtain patent protection. There may be prior art of which we are not aware that may affect the breadth, validity or enforceability of our patents and patent applications. There also may be prior art of which we are aware, but which we do not believe affects the breadth, validity or enforceability of our patents, which may, nonetheless, ultimately be found to affect the breadth, validity or enforceability of our patents. The patent applications we own or license may fail to result in issued patents in the United States or in foreign countries. Third parties may challenge the inventorship, ownership, breadth, validity, or enforceability of any issued patents we own or license or any patent applications that may issue as patents in the future, which may result in those patents being narrowed, invalidated or held unenforceable or the patent applications failing to issue as patents. Even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from developing similar products that do not fall within the scope of our patents. We may be required to disclaim part or all of the subject matter and/or term of certain patents or all of the subject matter and/or patent term of certain of our patents and patent applications. If the inventorship, ownership, breadth, validity, or enforceability of the patents we own or license is threatened, our ability to effectively commercialize any product candidates with technology protected by those patents could be threatened. Further, if we encounter delays in our clinical trials, the period of time during which we would have patent protection for any covered product candidates after obtaining regulatory approval would likely be reduced. Since patent applications filed in the United States and most other countries are confidential for a period of time after filing, we cannot be certain at the time of filing such applications that we or our licensors are the first to file any patent application related to our product candidates.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our 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 United States Patent and Trademark Office, or 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 patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition and prospects.

Our license agreements relating to our entrectinib, RXDX-105, RXDX-106 and taladegib development programs grant us exclusive, worldwide licenses under a portfolio of patents and patent applications directed to the licensed development programs. We own the rights to composition of matter patents and patent applications directed to our RXDX-106 and RXDX-107 programs. The composition of matter patents in the United States expire in 2029 for the issued patent relating to entrectinib, in 2030 for the issued patent relating to RXDX-105, in 2032 for the issued patent relating to RXDX-106, in 2033 for the issued patent relating to RXDX-107, and in 2031 for the issued patent relating to taladegib. While patent term extensions under the Hatch-Waxman Act in the United States and under supplementary protection certificates in Europe may be available to extend our patent exclusivity for any of these product candidates, the applicable patents may not meet the specified conditions for eligibility for any such term extension and, even if eligible, we may not be able to obtain any such term extension. Further, we may elect to pursue patent protection relating to our product candidates only in certain jurisdictions. As a result, competitors would be permitted to use our technologies in jurisdictions where we have not obtained patent protection to develop their own products, any of which could compete with our product candidates.

Inventions, and the intellectual property rights covering them, that are discovered under research, material transfer or other such collaboration agreements may become solely owned by us in some cases, jointly owned by us and the other party to such agreements in some cases, and may become the exclusive property of other party to such agreements in other cases. Under some circumstances, it may be difficult to determine which party owns a particular invention, or whether it is jointly owned, and disputes could arise regarding ownership of those inventions. These disputes could be costly and time consuming and an unfavorable outcome could have a significant adverse effect on our business if we were not able to protect or license rights to these inventions. In addition, our research collaborators may have contractual rights that permit them to use our proprietary compounds for specific studies, and publish our data and other proprietary information, subject to our prior review. Unauthorized uses of our proprietary compounds by such research collaborators, and publications by our research collaborators and scientific advisors containing such information, either with our permission or in contravention of the terms of their agreements with us, may limit or foreclose our ability to obtain patent protection for our product candidates or protect our proprietary information, which could materially harm our business, prospects, financial condition and results of operations.

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In addition, issued patents and pending patent applications require regular maintenance and payment of taxes, fees and/or annuities in several stages over the lifetime of the patents and patent applications. We employ an outside firm and rely on our outside counsel to pay these fees when they are due. We, the outside firm or our outside counsel could inadvertently abandon a patent or patent application due to non-payment of such taxes, fees and/or annuities, or as a result of a failure to comply with filing deadlines or other requirements of the prosecution process, resulting in the loss of protection of certain intellectual property rights in a certain country. Alternatively, we, our collaborators, or our patent counsel may take action resulting in a patent or patent application becoming abandoned which may not be able to be reinstated, or if reinstated, may result in a reduction of patent term. Failure to maintain our portfolio may result in loss of rights that may adversely impact our intellectual property rights, for example by rendering issued patents lapsed, void, or unenforceable, prematurely terminating pending applications, or reducing patent term.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, inventions for which patents are difficult to enforce and any other elements of our discovery platform and drug development processes that involve proprietary know-how, information or technology that is not covered by patents or not amenable to patent protection. Although we require all of our employees and certain consultants and advisors to assign inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, our trade secrets and other proprietary information may be disclosed or competitors may otherwise gain access to such information or independently develop substantially equivalent information. 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, courts outside the United States are sometimes less willing to protect trade secrets. Moreover, if our competitors independently develop equivalent knowledge, methods or know-how, it will be more difficult or impossible for us to enforce our rights and our business could be materially harmed. Any disclosure to or misappropriation by third parties of our trade secret or other confidential information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding any competitive advantage we may derive from this information.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant difficulty in protecting and defending our intellectual property both in the United States and abroad. If we are unable to effectively utilize our intellectual property to protect our products, we may not be able to establish or maintain the competitive advantage that we believe is provided by such intellectual property, which could materially and adversely affect our market position and business and operational results.

Claims that we infringe the intellectual property rights of others may prevent or delay our drug development efforts.

Our research, development and commercialization activities, as well as any product candidates or products resulting from those activities, may infringe or be alleged to infringe a patent or other form of intellectual property under which we do not hold a license or other rights. Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents of which we are currently unaware with claims that cover the composition of matter, use or manufacture of our product candidates or the practice of our related methods. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that our product candidates, their use, and manufacture or our related methods may infringe. In addition, third parties may obtain patents in the future and claim that our product candidates, their use, and manufacture or our related methods infringe one or more claims of these patents. If our activities or product candidates are determined to infringe the patents or other intellectual property rights of third parties, the holders of such intellectual property rights may be able to block our ability to develop and commercialize such product

candidates or practice our methods unless we obtain a license under the intellectual property rights or until any applicable patents expire or are determined to be invalid or unenforceable.

Defense of any intellectual property infringement claims against us, regardless of their merit, would involve substantial litigation expense and would be a significant diversion of employee resources and distract management from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties, limit our business to avoid the infringing activities, pay royalties and/or redesign our infringing product candidates or methods, any or all of which may be impossible or require substantial time and monetary expenditure. Although we carry general liability insurance, our insurance does not cover potential claims of this type. The occurrence of any of the above events could prevent us from continuing to develop and commercialize one or more of our product candidates or practice our related methods, and our business could materially suffer.

Many of our collaboration agreements are complex and may call for licensing or cross-licensing of potentially blocking patents, know-how or intellectual property. Due to the potential overlap of data, know-how and intellectual property rights there can be no assurance that one of our collaborators will not dispute our right to send data or know-how or other intellectual property rights to third parties and this may potentially lead to liability or termination of a program or litigation. There are no assurances that the actions of our

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collaborators would not lead to disputes or cause us to default with other collaborators. We cannot be certain that a collaborator will not challenge the validity of licensed patents.

We may desire, or be forced, to seek additional licenses to use intellectual property owned by third parties, and such licenses may not be available on commercially reasonable terms or at all.

A third party may hold intellectual property, including patent rights, that are important or necessary to the development or commercialization of our product candidates or to practice our related methods, in which case we would need to obtain a license from that third party or develop a different method relating to the product candidate that does not infringe the applicable intellectual property, which may not be possible. Additionally, we may identify product candidates that we believe are promising and whose composition of matter, use or manufacture are covered by the intellectual property rights of third parties. In such a case, we may desire to seek a license to pursue the development and commercialization of those product candidates. Any license that we may desire to obtain, or that we may be forced to pursue, may not be available when needed on commercially reasonable terms, or at all. Any inability to secure a license that we need or desire could have a material adverse effect on our business, financial condition and prospects.

The patent protection covering some of our product candidates may be dependent on third parties, who may not effectively maintain that protection.

While we expect that we will generally seek to gain the right to fully prosecute and maintain any issued patents and pending patent applications covering product candidates we may in-license from third-party owners, there may be instances when the prosecution and maintenance of issued patents and pending patent applications that cover our product candidates remain controlled by our licensors. For instance, NMS has retained certain patent prosecution and maintenance rights under our license agreements relating to our entrectinib program, Daiichi Sankyo holds certain patent prosecution and maintenance rights under our license agreement relating to our RXDX-105 and RXDX-106 programs, and Lilly holds certain patent prosecution and maintenance rights under our license agreement relating to our taladegib programs. If any of our current or future licensing partners that retain the right to prosecute and maintain patents and pending patent applications covering the product candidates we license from them fail to appropriately prosecute and maintain that patent protection, we may not be able to prevent competitors from developing and selling competing products or practicing competing methods, and our ability to generate revenue from any commercialization of the affected product candidates may suffer.

We may be involved in lawsuits or administrative proceedings to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe our patents or the patents of our current or potential licensors. We cannot predict if, when or where a third party may infringe one or more of our issued patents. To attempt to stop infringement or unauthorized use, we may need to enforce one or more of our patents, which can be expensive and time-consuming, a significant diversion of employee resources, and distract our management. There is no assurance such action will ultimately be successful in halting third party infringing activities, for example, through a permanent injunction, or that we would be fully or even partially financially compensated for any harm to our business caused by such third party infringement. Even if such action were initially successful, it could be overturned upon appeal. Even if we are successful in proving in a court of law that a third party is infringing one or more of our issued patents we may be forced to enter into a license or other agreement with the infringing third party on terms less commercially acceptable to us than if the license or agreement were negotiated under conditions between those of a willing licensee and a willing licensor. We may not become aware of a third party infringer within legal timeframes that would enable us to seek adequate compensation, or at all, thereby possibly losing the ability to be compensated for any harm to our

business. Such a third-party may be operating in a foreign country where the infringer is difficult to locate, where we do not have issued patents and/or the patent laws may be more difficult to enforce. If we pursue any litigation, a court may decide that a patent of ours or our licensor s is not of sufficient breath, is invalid, or is unenforceable, or may refuse to stop the other party from using the relevant technology on the grounds that our patents do not cover the technology in question. Further, the legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, which could reduce the likelihood of success of any infringement proceeding we pursue in any such jurisdiction. An adverse result in any patent litigation could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our pending patent applications at risk of not issuing, which could limit our ability to exclude competitors from directly competing with us in the applicable jurisdictions.

Certain administrative proceedings may be provoked by third parties before the USPTO and certain foreign patent offices, such as interference proceedings, opposition proceedings, re-examination proceedings, *inter partes* review, post-grant review, derivation proceedings and pre-grant submissions, in which third parties may challenge the validity or breadth of claims contained in our patents or those of our licensors. An adverse result in any such administrative proceeding could put one or more of our patents at risk of being

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canceled or invalidated or interpreted narrowly and could put our pending patent applications at risk of not issuing, which could limit our ability to exclude competitors from directly competing with us in the applicable jurisdictions.

Interference proceedings provoked by third parties or brought by us or the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. Derivation proceedings may be brought by us or a third party to determine whether a patent or application was filed by the true inventor. An unfavorable outcome in an interference or derivation proceeding could require us to cease using the related technology or to attempt to license rights to use it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, or at all. Litigation, interference, or derivation proceedings may have undesirable outcomes and, even if successful, may result in substantial costs, be a significant diversion of employee resources, and distract our management.

Risks Related to Managing Any Growth We May Experience

We will need to grow the size of our organization, and we may experience difficulties in managing any growth we may achieve.

As of February 28, 2017, we had 112 employees, 108 of whom were full-time and four of whom were part-time employees. As our development and commercialization plans and strategies develop, we expect to need additional research, development, managerial, operational, sales, marketing, financial, accounting, legal and other resources. We expect future growth to impose significant added responsibilities on members of management, particularly as we continue to expand our ongoing entrectinib and other development programs including:

effectively managing our clinical trials and submissions to regulatory authorities for marketing approvals;

effectively managing our preclinical development efforts;

identifying, recruiting, maintaining, motivating and integrating additional employees;

establishing relationships with third parties essential to our business and ensuring compliance with our contractual obligations to such third parties;

developing and managing new segments of our internal business, including any sales, marketing and commercial operations functions we may elect to establish;

maintaining our compliance with public company reporting and other obligations, including establishing and maintaining effective internal control over financial reporting and disclosure controls and procedures; and

improving our managerial, development, operational and finance systems. We may not be able to accomplish any of those tasks, and our failure to do so could prevent us from effectively managing future

growth, if any, and successfully growing our company.

We may in the future be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws, physician payments transparency and health information privacy and security laws. If we are unable to comply with any such laws, we could face substantial penalties.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations will be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, anti-kickback and false claims statutes. These laws may impact, among other things, any sales, marketing and education programs we may develop in the future and the manner in which we implement any of those programs, and include the following:

the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs, such as the Medicare and Medicaid programs. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation; in addition, 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 False Claims Act;

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federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid or other federal third-party payers that are false or fraudulent;

federal criminal laws that prohibit executing a scheme to defraud any federal healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it to have committed a violation;

the federal Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information;

the federal Physician Payment Sunshine Act, 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 CMS 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 requires applicable manufacturers and group purchasing organizations to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members and payments or other transfers of value to such physician owners. Manufacturers are required to submit reports to the government by the 90th day of each calendar year;

analogous state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry s voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state 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 and pricing information; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The risk of our being found in violation of these laws is increased by the fact that many of them have not been fully interpreted by the regulatory authorities or the courts, and their provisions are open to a variety of interpretations. Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available under such laws, it is possible that some of our business activities, including our relationships with physicians and other healthcare providers, some of whom will recommend, purchase and/or prescribe our products, could be subject to challenge under one or more of such laws.

If our operations are found to be in violation of any of those laws or any other governmental regulations that may apply to us in connection with marketing and sales of any product candidates that may gain regulatory approval, we may be subject to penalties, including civil and criminal penalties, damages, fines, exclusion from government healthcare programs and/or the curtailment or restructuring of our operations, any of which could adversely affect our

ability to operate our business and our financial condition.

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of any hazardous materials we use and wastes we produce. The use of these materials in our business could result in contamination or injury, which could cause damage for which we may be responsible but may not have sufficient resources to pay. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with these laws and regulations, which we may not be able to afford.

Although we maintain workers compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

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In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts or impact the research activities we pursue, particularly with respect to research involving human subjects or animal testing. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions, which could cause our financial condition to suffer.

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

We have incurred substantial losses during our history and do not expect to become profitable in the foreseeable future and may never achieve profitability. To the extent we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Section 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change (generally defined as a cumulative change in equity ownership by 5% shareholders that exceeds 50 percentage points over a rolling three-year period), the corporation s ability to use its pre-ownership change net operating loss carryforwards and other pre-ownership change tax attributes to offset its post-ownership change income and taxes may be limited. We may have experienced an ownership change as a result of our October 31, 2013 merger transaction, our November 2013, March 2014, March 2015, June 2015 and May 2016 common stock offerings, our March 2015 transaction with Teva and our November 2015 transaction with Lilly, and we may experience one or more ownership changes as a result of future transactions in our stock. We have not performed, nor do we have any current plan to perform, a formal study of such potential limitations on the use of our net operating loss carryforwards and other tax assets. As a result, we may be limited in our ability to use our net operating loss carryforwards and other tax assets to reduce taxes owed on the net taxable income that we earn. As of December 31, 2016, we believe we had federal and state net operating loss carryforwards of approximately $192.3 million and $138.8 million, respectively. These net operating loss carryforwards could be limited if the merger, the common stock offerings or the Teva and Lilly transactions resulted in an ownership change, or if we experience any other ownership change, which could potentially result in increased future tax liability to us. In addition, we are reporting an uncertain tax position in respect of approximately $83.3 million of our California state net operating loss carryforward, which carryforward would be disallowed unless a recent California Supreme Court decision on apportionment is overturned.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and we may incur substantial costs to attempt to recover or reproduce the data. If any disruption or security breach resulted in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and/or the further development of our product candidates could be delayed.

Our operations are vulnerable to interruption by natural disasters, power loss, terrorist activity and other events beyond our control, the occurrence of which could materially harm our business.

Businesses located in California have, in the past, been subject to electrical blackouts as a result of a shortage of available electrical power, and any future blackouts could disrupt our operations. We are vulnerable to a major earthquake, wildfire, flooding, inclement weather and other natural disasters, and we have not undertaken a systematic analysis of the potential consequences to our business as a result of any such natural disaster and do not have an

applicable recovery plan in place. We carry only limited business interruption insurance that would compensate us for actual losses from interruption of our business that may occur, and any losses or damages incurred by us in excess of insured amounts could cause our business to materially suffer.

Risks Related to Ownership of Our Common Stock

There may not be a viable trading market for our common stock, which may make it difficult for you to sell your shares.

Our common stock had not been publicly traded on the NASDAQ Capital Market prior to our public offering in March 2014. The trading market for our common stock on the NASDAQ Capital Market has been limited, and an active trading market for our shares may not be sustained. As a result of these and other factors, you may be unable to sell your shares at a price that is attractive to you, or at all. Further, an inactive trading market may also impair our ability to raise capital by selling shares of our common stock in the

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future, and may impair our ability to enter into strategic partnerships or acquire companies or products by using shares of our common stock as consideration.

Our share price is volatile and may be influenced by numerous factors, some of which are beyond our control.

The price for our common stock currently is, and is likely to continue to be, highly volatile, and could be subject to wide fluctuations. That price fluctuation could be in response to various factors, some of which may be beyond our control. These factors are discussed in this Risk Factors section, and elsewhere in this Annual Report on Form 10-K, as updated by our subsequent filings under the Exchange Act. These factors include, without limitation:

- the product candidates we pursue, and our ability to obtain rights to develop, commercialize and market those product candidates;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial or development program;
- actual or anticipated adverse results or delays in our clinical trials;
- our failure to successfully commercialize our product candidates, if approved, either ourselves or through one or more collaborators;
- unanticipated serious safety concerns related to the use of any of our product candidates;
- adverse regulatory decisions;
- additions or departures of key scientific or management personnel;
- changes in laws or regulations applicable to our product candidates, including without limitation clinical trial requirements for approvals;
- disputes or other developments relating to patents and other proprietary rights and our ability to obtain patent and other intellectual property protection for our product candidates;
- our dependence on third parties, including CROs and contract manufacturers, as well as our potential partners that may produce companion diagnostic products or commercialization capabilities;

failure to meet or exceed any financial guidance or expectations regarding development milestones that we may provide to the public;

actual or anticipated variations in quarterly operating results, liquidity or other indicators of our financial condition;

failure to meet or exceed the estimates and projections of the investment community;

overall performance of the equity markets and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;

conditions or trends in the biotechnology and biopharmaceutical industries;

announcements of achievement of development or regulatory milestones, or the introduction of new products offered by us or our competitors;

announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;

our ability to maintain an adequate rate of growth and manage such growth;

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issuances of debt or equity securities;

sales of our common stock by us or our stockholders in the future, or the perception that such sales could occur;

trading volume of our common stock;

ineffectiveness of our internal control over financial reporting or disclosure controls and procedures;

general political and economic conditions;

effects of natural or man-made catastrophic events; and

other events or factors, many of which are beyond our control.

In addition, the stock market in general, and the stocks of small-cap biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these 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 could have a dramatic and material adverse impact on the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public market, or the perception that such sales could occur, could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of February 28, 2017, a total of 41,700,063 shares of our common stock were outstanding. Of those shares, approximately 37,389,300 were freely tradable, without restriction, in the public market. Such shares represented approximately 90% of our outstanding shares of common stock as of that date. Any sales of those shares or any perception in the market that such sales may occur could cause the trading price of our common stock to decline.

In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our equity incentive plans will be eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, Rule 144 and Rule 701 under the Securities Act of 1933, as amended, or the Securities Act, our effective Registration Statements on Form S-8 and any future registration of such shares under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

The resale of shares covered by our effective resale registration statements could adversely affect the market price of our common stock in the public market, which result could in turn negatively affect our ability to raise additional equity capital.

The sale, or availability for sale, of our common stock in the public market may adversely affect the prevailing market price of our common stock and may impair our ability to raise additional equity capital. We filed registration statements with the SEC to register the resale of all of the 3,000,000 shares of our common stock issued and sold to Teva in March 2015, and all of the 2,713,000 shares of our common stock issued and sold to Lilly in November 2015. Both of these registration statements have been declared effective by the SEC. The resale registration statements permit the resale of these shares at any time without restriction. The resale of a substantial number of shares of our common stock in the public market could adversely affect the market price for our common stock and make it more difficult for you to sell shares of our common stock at times and prices that you feel are appropriate. Furthermore, because there are a large number of shares registered pursuant to the resale registration statements, the selling stockholders named in such registration statements may continue to offer shares covered by the resale registration statements for a significant period of time, the precise duration of which cannot be predicted. Accordingly, the adverse market and price pressures resulting from an offering pursuant to the resale registration statements may continue for an extended period of time, and continued negative pressure on the market price of our common stock could have a material adverse effect on our ability to raise additional equity capital.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans or otherwise, could result in dilution to the percentage ownership of our stockholders and could cause our stock price to fall.

We expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities, previous investors may be materially diluted. Additionally, new investors could gain rights, preferences and privileges senior to those of existing holders of our common

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stock. Further, any future sales of our common stock by us or resales of our common stock by our existing stockholders could cause the market price of our common stock to decline. In addition, any future grants of options, warrants or other securities exercisable or convertible into our common stock, or the exercise or conversion of such shares, and any sales of such shares in the market, could have an adverse effect on the market price of our common stock.

We incur significant costs associated with, and our management is required to devote substantial time and effort to, compliance with public company reporting and other requirements.

As a public company listed on the NASDAQ Capital Market, we incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as the rules and regulations of the SEC and the NASDAQ Capital Market, impose numerous requirements on public companies, including requirements relating to effective disclosure and financial controls and changes in corporate governance practices, with which we need to comply. Further, since we are subject to the Exchange Act, we are required to, among other things, file annual, quarterly and current reports with respect to our business and operating results. Our management and other personnel will need to devote substantial time to operations as a public company and compliance with applicable laws and regulations, and our efforts and initiatives to comply with those requirements could be expensive and may include hiring additional legal, financial reporting and other finance and accounting staff and engaging consultants to assist in designing and implementing such procedures. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss and may require us to reduce costs in other areas of our business or increase the prices of our products or services. Further, stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

If we fail to maintain proper and effective internal controls, our ability to produce accurate and timely financial statements could be impaired, which could harm our operating results, our ability to operate our business and investors views of us.

We are required to comply with certain aspects of Section 404 of the Sarbanes-Oxley Act. Section 404 of the Sarbanes-Oxley Act requires public companies to, among other things, conduct an annual review and evaluation of their internal controls over financial reporting. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will require frequent evaluation. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock. In addition, if our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

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

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of securities or industry analysts covering our business downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely

decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

We are an emerging growth company, allowing us to take advantage of certain reduced disclosure obligations as a public reporting company that may make our common stock less attractive to investors. Additionally, as an emerging growth company, we have elected to delay the adoption of new or revised accounting pronouncements applicable to public companies until such pronouncements are made applicable to private companies.

We are an emerging growth company under the Jumpstart Our Business Startups Act, or the JOBS Act. Accordingly, we are eligible to take advantage of certain extended accounting standards and exemptions from various reporting requirements that are not available to public reporting companies that do not qualify for this classification. For instance, we are not required to hold a nonbinding advisory stockholder vote on executive compensation or any golden parachute payments not previously approved by stockholders; we are not required to comply with the requirement of auditor attestation of management s assessment of internal control over financial reporting, which is required for some other public reporting companies by Section 404 of the Sarbanes-Oxley Act of 2002; and we are eligible for reduced financial statement disclosure in any registration statements under the Securities Act or reports under the

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Exchange Act that we may file. For as long as we continue to be an emerging growth company, which we anticipate will be for the foreseeable future, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of this classification. As a result, our publicly available disclosure may not be as robust or comprehensive as that of other public reporting companies that do not qualify for this classification.

Further, as an emerging growth company, we can elect to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected to take advantage of this extended transition period. Since we will not be required to comply with new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies, our financial statements may not be comparable to the financial statements of other public companies that comply with the effective dates of those accounting standards.

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.

Certain of our executive officers, directors and large stockholders own a significant percentage of our outstanding capital stock. As of February 28, 2017, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 54% of our outstanding voting stock (which includes shares they had the right to acquire within 60 days). Accordingly, our directors and executive officers and large stockholders have significant influence over our affairs due to their substantial ownership coupled with the positions of some of these stockholders on our management team, and have substantial voting power to approve matters requiring the approval of our stockholders. 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 concentration of ownership in our Board of Directors and management team and certain other large stockholders may prevent or discourage unsolicited acquisition proposals or offers for our common stock that some of our stockholders may believe are in their best interest.

If we issue additional shares of our capital stock in the future, our existing stockholders will be diluted.

Our second amended and restated certificate of incorporation authorizes the issuance of up to 150,000,000 shares of our common stock and up to 10,000,000 shares of preferred stock with the rights, preferences and privileges that our board of directors may determine from time to time. In addition to capital raising activities such as public and private placements of our common stock, other possible business and financial uses for our authorized capital stock include, without limitation, future stock splits, acquiring other companies, businesses or products in exchange for shares of our capital stock, issuing shares of our capital stock to partners or other collaborators in connection with strategic alliances, attracting and retaining employees by the issuance of additional securities under our equity compensation plans, or other transactions and corporate purposes that our board of directors deems are in the best interest of our company and our stockholders. Additionally, shares of our capital stock could be used for anti-takeover purposes or to delay or prevent changes in control or our management. Any future issuances of shares of our capital stock may not be made on favorable terms or at all, they may not enhance stockholder value, they may have rights, preferences and privileges that are superior to those of our common stock, and they may have an adverse effect on our business or the trading price of our common stock. The issuance of any additional shares of our common stock will reduce the book value per share and may contribute to a reduction in the market price of the outstanding shares of our common stock. Additionally, any such issuance will reduce the proportionate ownership and voting power of all of our current stockholders.

Anti-takeover provisions under our charter documents and Delaware law could delay or prevent a change of control which could limit the market price of our common stock and may prevent or frustrate attempts by our

stockholders to replace or remove our current management.

Our second amended and restated certificate of incorporation and amended and restated bylaws contain provisions that could delay or prevent a change of control of our company or changes in our board of directors that our stockholders might consider favorable. Some of these provisions include:

a board of directors divided into three classes serving staggered three-year terms, such that not all members of the board will be elected at one time;

a prohibition on stockholder action through written consent, which requires that all stockholder actions be taken at a meeting of our stockholders;

a requirement that special meetings of stockholders be called only by the chairman of the board of directors, the chief executive officer, the president or by a majority of the total number of authorized directors;

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advance notice requirements for stockholder proposals and nominations for election to our board of directors;

a requirement that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of all outstanding shares of our voting stock then entitled to vote in the election of directors;

a requirement of approval of not less than two-thirds of all outstanding shares of our voting stock to amend any bylaws by stockholder action or to amend specific provisions of our second amended and restated certificate of incorporation; and

the authority of the board of directors to issue preferred stock on terms determined by the board of directors without stockholder approval and which preferred stock may include rights superior to the rights of the holders of common stock.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporate Law, which may prohibit certain business combinations with stockholders owning 15% or more of our outstanding voting stock. These anti-takeover provisions and other provisions in our second amended and restated certificate of incorporation and amended and restated bylaws could make it more difficult for stockholders or potential acquirers to obtain control of our board of directors or initiate actions that are opposed by the then-current board of directors and could also delay or impede a merger, tender offer or proxy contest involving our company. These provisions could also discourage proxy contests and make it more difficult for you and other stockholders to elect directors of your choosing or cause us to take other corporate actions you desire. Any delay or prevention of a change of control transaction or changes in our board of directors could cause the market price of our common stock to decline.

We do not intend to pay cash dividends on our capital stock in the foreseeable future.

Other than a $3.50 per share cash dividend we declared and paid in connection with and prior to the closing of the October 31, 2013 merger in which we initially became the wholly owned subsidiary of the company previously known as Infinity Oil & Gas Company, we have never declared or paid any dividends on our common stock and do not anticipate paying any dividends in the foreseeable future. In addition, our ability to pay cash dividends is currently prohibited by the terms of our loan agreement with SVB and Oxford. Any future payment of cash dividends would depend on our financial condition, contractual restrictions, solvency tests imposed by applicable corporate laws, our results of operations, our anticipated cash requirements and other factors and will be at the discretion of our board of directors. Our stockholders should not expect that we will ever pay cash or other dividends on our outstanding capital stock.

The results of the United Kingdom s referendum on withdrawal from the European Union, or EU, may have a negative effect on global economic conditions, financial markets and our business.

On June 23, 2016, a majority of voters in the United Kingdom elected to withdraw from the EU in a national referendum (commonly referred to as Brexit). The referendum was advisory, and the terms of any withdrawal are subject to a negotiation period that could last at least two years after the government of the United Kingdom formally initiates a withdrawal process. Nevertheless, the referendum has created significant uncertainty about the future relationship between the United Kingdom and the EU, and has given rise to calls for certain regions within the United

Kingdom to preserve their place in the EU by separating from the United Kingdom, as well as for the governments of other EU member states to consider withdrawal.

These developments, or the perception that any of them could occur, have had and may continue to have a material adverse effect on global economic conditions and the stability of global financial markets, and could significantly reduce global market liquidity and restrict the ability of key market participants to operate in certain financial markets. Asset valuations, currency exchange rates and credit ratings may be especially subject to increased market volatility. Lack of clarity about future U.K. laws and regulations as the United Kingdom determines which EU laws to replace or replicate in the event of a withdrawal, including financial laws and regulations, tax and free trade agreements, intellectual property rights, supply chain logistics, environmental, health and safety laws and regulations, immigration laws and employment laws, could decrease foreign direct investment in the United Kingdom, increase costs and depress economic activity. If the United Kingdom and the EU are unable to negotiate acceptable withdrawal terms or if other EU member states pursue withdrawal, barrier-free access between the United Kingdom and other EU member states or among the European economic area overall could be diminished or eliminated. In addition, we expect that Brexit could lead to legal uncertainty and potentially divergent national laws and regulations as the United Kingdom determines which EU laws to replicate or replace. If the United Kingdom were to significantly alter its regulations affecting the biotechnology or pharmaceutical industries, we could face significant new costs. It may also be time-consuming and expensive for us to alter our internal operations in order to comply with new regulations. Altered regulations could also add time and expense to the process by which our product candidates receive regulatory

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approval in the United Kingdom and the EU. Similarly, it is unclear at this time what Brexit s impact will have on our intellectual property rights and the process for obtaining and defending such rights. It is possible that certain intellectual property rights, such as trademarks, granted by the EU will cease being enforceable in the United Kingdom absent special arrangements to the contrary. With regard to existing patent rights, the effect of Brexit should be minimal considering enforceable patent rights are specific to the United Kingdom, whether arising out of the European Patent Office or directly through the U.K. patent office. Any of these factors could have a material adverse effect on our business, financial condition and results of operations and affect our strategy in the U.K. pharmaceutical market.

We may have material liabilities that were not discovered before, and have not been discovered since, the closing of our October 2013 merger.

As a result of the October 31, 2013 merger in which we initially became the wholly owned subsidiary of the company previously known as Infinity Oil & Gas Company, the former business plan and management of such company were abandoned and replaced with our business and management team. Prior to the merger, there were no relationships or other connections among the businesses or individuals associated with those two entities. As a result, we may have material liabilities based on activities before the merger that have not been discovered or asserted. We could experience losses as a result of any such undisclosed liabilities that are discovered in the future, which could materially harm our business and financial condition. Although the merger agreement entered into in connection with the merger contains customary representations and warranties from the former Infinity Oil & Gas Company concerning its assets, liabilities, financial condition and affairs, there may be limited or no recourse against that company s pre-merger stockholders or principals in the event those representations prove to be untrue. As a result, our current and future stockholders will bear some, or all, of the risks relating to any such unknown or undisclosed liabilities.

We may be exposed to additional risks as a result of going public by means of a reverse merger transaction.

We may be exposed to additional risks because we became a public company through a reverse merger transaction. There has been increased focus in recent years by government agencies on transactions such as this reverse merger transaction, and we may be subject to increased scrutiny and/or restrictions by the SEC and other government agencies and holders of our securities as a result of the completion of that transaction. Additionally, our going public by means of a reverse merger transaction may make it more difficult for us to obtain coverage from securities analysts of major brokerage firms because there may be little incentive to those brokerage firms to recommend the purchase of our common stock. The occurrence of any such event could cause our business or stock price to suffer.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Under a ten-year lease which commenced in October 2016, we lease approximately 97,000 rentable square feet of office and laboratory space in two separate buildings in San Diego, California with monthly rent payments of approximately $359,000 although the first eight months of base rent are abated. We also lease approximately 8,200 rentable square feet of laboratory space in a separate building in San Diego, California with monthly rent payments of approximately $22,000 which lease will be terminated shortly after moving the laboratory functions housed there to

our main office and laboratory building in the second quarter of 2017. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings

We are not currently a party to, nor is our property the subject of, any material legal proceedings.

Item 4. Mine Safety Disclosures

Not Applicable.

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PART II

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

Market Information

Our common stock is listed on the NASDAQ Capital Market under the ticker symbol RXDX. As of February 28, 2017, the closing sales price for our common stock as reported on the NASDAQ Capital Market was $8.80 per share.

The table below sets forth reported high and low sales prices for our common stock for the fiscal quarters indicated as reported on NASDAQ.

	High	Low
2015:		
First Quarter	$ 10.73	$ 6.41
Second Quarter	19.40	8.28
Third Quarter	18.19	8.07
Fourth Quarter	15.20	8.08
2016:		
First Quarter	$ 13.41	$ 5.07
Second Quarter	9.69	4.63
Third Quarter	6.72	5.25
Fourth Quarter	7.20	4.15
2017:		
First Quarter (through February 28, 2017)	$ 9.70	$ 4.60

Holders

As of February 28, 2017, there were 93 registered holders of record of our common stock.

Dividends

In connection with and prior to the closing of the merger in which we became a wholly owned subsidiary of Ignyta, Inc., or Parent, a Nevada corporation previously named Infinity Oil & Gas Company, on October 31, 2013, Parent declared a $3.50 per share cash dividend to its common stockholders of record as of that date and time. Other than the dividend declared in connection with the merger, we have never declared nor paid any cash dividends to stockholders. We do not intend to pay cash dividends on our common stock for the foreseeable future, and we currently intend to retain any future earnings to fund our operations and the development and growth of our business. The declaration of any future cash dividend, if any, would be at the discretion of our Board of Directors and would depend upon our earnings, if any, our capital requirements and financial position, our general economic conditions, and other pertinent conditions. In addition, our ability to pay dividends is currently restricted by the terms of the loan agreement with SVB and Oxford.

Securities Authorized for Issuance Under Equity Compensation Plan

Information about our equity compensation plans is incorporated by reference in Item 12 of Part III of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities

None.

Issuer Repurchases of Equity Securities

None.

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Stock Performance Graph

The graph below shows the cumulative total stockholder return assuming the investment of $100 on March 14, 2014 (and the reinvestment of dividends thereafter) in each of (a) Ignyta, Inc. s common stock, (b) the NASDAQ Composite Index and (c) the NASDAQ Biotechnology Index. The Comparisons in the graph below are based on historical data and are not indicative of, or intended to forecast, future performance of our common stock or of the Indexes.

	03/14/14	12/31/14	12/31/15	12/30/16
Ignyta, Inc	$ 100.00	$ 67.16	$ 131.37	$ 51.96
Nasdaq Bio Index	$ 100.00	$ 119.84	$ 133.53	$ 104.57
Nasdaq Comp Index	$ 100.00	$ 111.56	$ 117.95	$ 126.80

The information contained in this Performance Graph section shall not be deemed soliciting material or to be filed with the SEC, for purposes of Section 18 of the Exchange Act, or otherwise subject to the liabilities under that Section, and shall not be deemed to be incorporated by reference into any filing of Ignyta, Inc. under the Securities Act or the Exchange Act.

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Item 6. Selected Financial Data.

The following selected financial data has been derived from our audited financial statements. This data should be read in conjunction with Item 7 Management s Discussion and Analysis of Financial Condition and Results of Operations and our financial statements and related notes thereto included elsewhere in this Form 10-K.

Our historical results are not necessarily indicative of operating results to be expected in the future.

	Years Ended December 31,			
Amounts in thousands, except per share data:	**2016**	**2015**	**2014**	**2013**
Statement of operations data:				
Research and development expenses (1)(2)	$ 76,926	$ 73,511	$ 30,505	$ 10,171
Total operating expenses	$ 100,684	$ 90,580	$ 40,011	$ 13,904
Loss from operations	$ (100,684)	$ (90,580)	$ (39,861)	$ (13,904)
Net loss	$ (103,639)	$ (92,458)	$ (39,990)	$ (14,214)
Net loss per share basic and diluted	$ (2.69)	$ (3.44)	$ (2.18)	$ (3.83)

	Years Ended December 31,			
Amounts in thousands, except per share data:	**2016**	**2015**	**2014**	**2013**
Balance sheet data:				
Cash, equivalents and investments	$ 132,960	$ 172,149	$ 76,634	$ 51,804
Working capital	$ 94,333	$ 111,450	$ 63,800	$ 50,944
Total assets	$ 144,914	$ 195,514	$ 85,306	$ 53,319
Total liabilities	$ (50,144)	$ (59,529)	$ (29,357)	$ (11,532)
Total stockholders equity	$ 94,770	$ 135,985	$ 55,949	$ 41,787

(1) Fiscal 2015 results include approximately $28.2 million of upfront expenses incurred in connection with our acquisition of rights to development programs consisting of the combined $25.3 million net value of our common stock issued and combined upfront payments totaling $2.9 million made to Teva and Lilly in connection with these transactions.

(2) Fiscal 2014 results include a $10.0 million milestone payment to NMS in connection with the entrectinib and RXDX-102 license agreement and a $3.5 million license fee paid to NMS for rights to the RXDX-103 and RXDX-104 product candidates.

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

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical information, this discussion and analysis contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including, but not limited, to those set forth under Item 1A Risk Factors and elsewhere in this Annual Report on Form 10-K.

On October 31, 2013, Ignyta, then known as Ignyta Operating, Inc., merged with and into IGAS Acquisition Corp., a wholly-owned subsidiary of Ignyta, Inc., or Parent, a Nevada corporation previously named Infinity Oil & Gas Company and formerly a shell company under applicable rules of the Securities and Exchange Commission. We survived the merger as a wholly owned subsidiary of Parent. In the merger, Parent acquired our business and continued our business operations. The merger is accounted for as a reverse merger and recapitalization, with Ignyta as the acquirer and Parent as the acquired company for financial reporting purposes. As a result, the assets and liabilities and the operations that are reflected in the historical financial statements prior to the merger are those of Ignyta and are recorded at the historical cost basis of Ignyta, and the financial statements after completion of the merger will include the assets and liabilities of Ignyta and Parent, the historical operations of Ignyta and the operations of the combined enterprise of Ignyta and Parent from and after the closing date of the merger. As a result of the accounting treatment of the merger and the change in Ignyta s business and operations from a shell company to a precision oncology biotechnology company, a discussion of the past financial results of the shell company is not pertinent or material, and the following discussion and analysis of our financial condition and results of operations are based on Ignyta s financial statements. On June 12, 2014, Parent merged with and into Ignyta, with Ignyta surviving the merger and changing its name to Ignyta, Inc.

Unless the context indicates or otherwise requires, the terms we, us, our and our company refer to (i) Ignyta for discussions relating to periods before and through the closing of the October 2013 merger, (ii) Parent and its consolidated subsidiary, Ignyta Operating, for discussions relating to periods after the closing of the October 2013 merger and before the closing of the June 2014 merger, and (iii) Ignyta for discussions relating to periods after the closing of the June 2014 merger.

Overview

We are a biotechnology company focused on precision medicine in oncology. Our goal is not just to shrink tumors, but to eradicate residual disease the source of cancer relapse and recurrence in precisely defined patient populations. We are pursuing an integrated therapeutic, or Rx, and companion diagnostic, or Dx, strategy for treating patients with cancer. Our Rx efforts are focused on in-licensing or acquiring, then developing and commercializing molecularly targeted therapies that, sequentially or in combination, are foundational for eradicating residual disease. Our Dx efforts aim to pair these product candidates with biomarker-based companion diagnostics that are designed to precisely identify, at the molecular level, the patients who are most likely to benefit from the therapies we develop.

Our current pipeline includes the following compounds:

entrectinib, formerly called RXDX-101, an orally bioavailable, CNS-active, small molecule tyrosine kinase inhibitor directed to the TRK (tropomyosin receptor kinase) family tyrosine kinase receptors (TRKA, TRKB and TRKC), ROS1 and ALK (anaplastic lymphoma kinase) proteins, which is in a Phase 2 clinical study and two Phase 1 clinical studies in molecularly defined adult patient populations for the treatment of solid tumors, and a Phase 1/1b clinical study in pediatric patients with advanced solid tumor malignancies;

RXDX-105, an orally bioavailable, VEGFR-sparing, small molecule tyrosine kinase inhibitor of RET, that has achieved clinical proof-of-concept and is in an ongoing Phase 1b clinical trial;

taladegib, an orally bioavailable, small molecule hedgehog/smoothened antagonist that has achieved clinical proof-of-concept and a recommended Phase 2 dose in a Phase 1 dose escalation trial; and

RXDX-106, a pseudo-irreversible, small molecule inhibitor of TYRO3, AXL and MER, or collectively TAM, and c-MET that is in late preclinical development.

We acquired exclusive global development and commercialization rights to entrectinib under a license agreement with Nerviano Medical Sciences S.r.l., or NMS, that became effective in November 2013; we acquired exclusive, global development and commercialization rights to taladegib under a license agreement with Eli Lilly and Company, or Lilly, in November 2015; and we

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acquired our RXDX-105 and RXDX-106 development programs in an asset purchase transaction with Cephalon, Inc., an indirect wholly-owned subsidiary of Teva Pharmaceutical Industries Ltd., or Teva, in March 2015.

In May 2016, we determined to prioritize our resources and development efforts on our lead product candidate, entrectinib. In connection with this, we determined to discontinue our Spark discovery-stage program and are in discussions with Lilly regarding the optimal path forward for taladegib in the context of our pipeline priorities. In connection with these discussions Lilly has indicated that it believes that we may not have satisfied certain of our obligations to Lilly under the license agreement, but Lilly has also indicated an interest in achieving an amicable resolution with respect to this issue and the parties are continuing discussions consistent with this desire.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, assembling our core capabilities in genetic and epigenetic based biomarker discovery, and developing drug candidates. Our product candidate development operations include preparing, managing and conducting preclinical and clinical studies and trials, preparing regulatory submissions relating to those product candidates and establishing and managing relationships with third parties in connection with all of those activities. We expect that in the future our operations may also, if regulatory approval is obtained, include pursuing the commercialization of our product candidates.

Financial Operations Overview

Revenue

To date, we have not generated any material revenue from services, product sales or otherwise. In the future, we expect that we will seek to generate revenue primarily from product sales, but we may also seek to generate revenue from research funding, milestone payments and royalties on future product sales in connection with any out-license or other strategic relationships we may establish.

Research and Development Expenses

The following table sets forth our research and development expenses for the periods presented (*in thousands*):

	Years ended December 31,		
	2016	**2015**	**2014**
Research and development expenses	$ 76,926	$ 73,511	$ 30,505

Research and development expenses consist primarily of costs incurred for our research activities, including our drug and biomarker discovery efforts and the development of our product candidates, which include:

- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, investigational sites and consultants;
- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;

the cost of acquiring, developing and manufacturing clinical study materials;

facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and laboratory and other supplies; and

license fees and other expenses relating to our acquisition of rights to our development programs.

Research and development costs are expensed as incurred. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

We do not track our employee and facility related research and development costs by project, as we typically use our employee and infrastructure resources across multiple research and development programs. We believe that the allocation of such costs would be arbitrary and would not be meaningful. We have not historically tracked external development costs by program as the majority of our development spend was focused on the development and clinical trials of entrectinib. We have contracted with CROs to manage our clinical trials under agreed upon budgets, with oversight by our clinical program managers. Any deviations from the budgets must be approved by us in writing. Our internal research and development costs are controlled through our internal budget and forecast process and subject to quarterly review and analysis of budget versus actual expenditures.

Research and development activities are central to our business model. Our research and development programs that we expect will be our focus in the immediate future consist of the development of our entrectinib, RXDX-105, taladegib, and RXDX-106 programs. Since product candidates in later stages of development generally have higher development costs than those in earlier stages of development, we expect research and development costs relating to each of those programs to increase significantly for the foreseeable future as those programs progress. However, the successful development of any of our product candidates, or any others

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we may seek to pursue, is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development for our programs, or whether any of our product candidates will reach successful commercialization. We are also unable to predict when, if ever, any net cash inflows will commence from any of the product candidates we currently or may in the future pursue. This lack of predictability is due to the numerous risks and uncertainties associated with developing medicines, many of which, such as our ability to obtain approvals to market and sell those medicines from the FDA, and other applicable regulatory authorities, are beyond our control, including the uncertainty of:

- establishing an appropriate safety profile with toxicology studies to submit an IND to the FDA or comparable applications to foreign regulatory authorities;
- successful enrollment in and adequate design and completion of clinical trials;
- successful demonstration of an acceptable safety profile with clinically meaningful efficacy to achieve a favorable benefit/risk profile sufficient to obtain regulatory approval in one or more countries;
- receipt of marketing approvals from applicable regulatory authorities, including the FDA and/or comparable foreign authorities;
- establishing commercial manufacturing capabilities or, more likely, seeking to establish arrangements with third-party manufacturers;
- obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;
- launching commercial sales of the products, if and when approved, including establishing an internal sales and marketing force and/or establishing relationships with third parties for such purpose;
- developing and commercializing, individually or with third-party collaborators, companion diagnostics; and
- a continued acceptable safety profile of the products following approval, if any.

A change in the outcome of any of these variables with respect to the development of any of our product candidates would significantly change the costs, timing and likelihood of success associated with the development of that product candidate.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and other related costs, including stock-based compensation, for personnel in executive, finance, accounting, business development, legal, commercial and human resources functions. Other significant costs include facility costs not otherwise included in research and development expenses, legal fees relating to patent and corporate matters and fees for accounting and consulting services.

We anticipate that our general and administrative expenses will increase in the future to support continued research and development activities, potential commercialization of our product candidates and increased costs of operating as a public company. These increases will likely include increased costs related to facilities expansion, the hiring of additional personnel and increased fees to outside consultants, lawyers and accountants, among other expenses. Additionally, increased costs associated with operating as a public company are expected to include expenses related to services associated with maintaining compliance with requirements of the SEC, insurance and investor relations costs.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of these financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of expenses during the reporting periods. We base our estimates on historical experience and on various other factors and assumptions that we believe are reasonable under the circumstances at the time the estimates are made, the results of which form the basis for making judgments about the book value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We periodically evaluate our estimates and judgments, including those described in greater detail below, in light of changes in circumstances, facts and experience.

Our critical accounting policies are those accounting principles generally accepted in the United States that require us to make subjective estimates and judgments about matters that are uncertain and are likely to have a material impact on our financial condition and results of operations, as well as the specific manner in which we apply those principles. Our significant accounting policies are described in more detail in the notes to our financial statements included in this Annual Report on Form 10-K. We believe the critical accounting policies used in the preparation of our financial statements that require significant estimates and judgments are as follows:

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Research and Development Expenses

Costs incurred in connection with research and development activities are expensed as incurred. Research and development expenses consist of (i) external research and development expenses incurred under arrangements with third parties, such as contract research organizations, investigational sites and consultants; (ii) employee-related expenses, including salaries, benefits, travel and stock compensation expense; (iii) the cost of acquiring, developing and manufacturing clinical study materials; (iv) facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and laboratory and other supplies, and (v) license fees and other expenses relating to the acquisition of rights to development programs.

We enter into consulting, research and other agreements with commercial firms, researchers, universities and others for the provision of goods and services. Under such agreements, we may pay for services on a monthly, quarterly, project or other basis. Such arrangements are generally cancellable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided to us by our clinical sites and vendors and other information. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on our behalf.

In certain circumstances, we are required to make advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the advance payments are deferred and are expensed when the activity has been performed or when the goods have been received.

Clinical Trial Accruals

We make estimates of accrued expenses as of each balance sheet date in our financial statements based on the facts and circumstances known to us at that time. Accrued expenses for clinical trials and pre-clinical studies are based on estimates of costs incurred and fees that may be associated with services provided by CROs, clinical trial investigational sites, and other related vendors. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and the completion of milestones. In accruing service fees, management estimates the time-period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate these services based on other information available to us. If we underestimate or overestimate the activity or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, estimated accrued liabilities have approximated actual expense incurred. Subsequent changes in estimates may result in a material change in our accruals.

Stock-Based Compensation

Stock-based compensation cost for equity awards to employees, consultants and members of our board of directors is measured at the grant date, based on the calculated fair value of the award using the Black-Scholes option-pricing model, and is recognized as an expense, under the straight-line method, over the requisite service period (generally the vesting period of the equity grant). Stock options issued to non-employees are accounted for at their estimated fair values determined using the Black-Scholes option-pricing model. The fair value of options granted to non-employees is re-measured as they vest, and the resulting increase in value, if any, is recognized as expense during the period the related services are rendered. Restricted stock issued to non-employees is accounted for at its estimated fair value as it vests.

In determining the fair value of the stock-based awards used to calculate stock-based compensation expense, we use the Black-Scholes option-pricing model and assumptions discussed below. Some of these inputs are subjective and require judgment to determine.

Expected Term. The expected term of stock options represents the weighted average period the stock options are expected to be outstanding. We have opted to use the simplified method for estimating the expected term as provided by authoritative literature as our options grants are considered plain vanilla . The simplified method calculates the expected term as the average time-to-vesting and the contractual life of the options. We plan to continue to use the simplified method until we have sufficient exercise history as a publicly traded company.

Expected Volatility. The expected stock price volatility assumption was determined by examining the historical volatilities of a group of industry peers, as we have limited trading history for our common stock. Industry peers consist of several public companies in the biopharmaceutical industry with comparable characteristics including enterprise value, risk profiles and position within the industry. We intend to continue to consistently apply this process using the same or similar public companies until sufficient historical information regarding the volatility of our own common stock share price is available, or unless circumstances change such that the identified companies are no longer similar to us, in which case, more suitable companies whose share prices are publicly available would be utilized in the calculation.

Risk-Free Interest Rate. The risk-free interest rate is based on the implied yield available on U.S. Treasury zero-coupon issues in effect at the time of grant for periods corresponding with the expected term of the option.

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Expected Dividend Yield. We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero for all years presented.

In addition to the Black-Scholes assumptions, we estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior and other factors. The impact from any forfeiture rate adjustment would be recognized in full in the period of adjustment, and if the actual number of future forfeitures differs from our estimates, we might be required to record adjustments to stock-based compensation in future periods.

Income Taxes

Deferred income taxes are recognized for the tax consequences in future years of differences between the tax basis of assets and liabilities and their financial reporting amounts at each year end based on enacted tax laws and statutory tax rates applicable to the periods in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized. Income tax expense is the combination of the tax payable for the year and the change during the year in deferred tax assets and liabilities. We follow the accounting guidance on accounting for uncertainty in income taxes. The guidance prescribes a recognition threshold and measurement attribute criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities based on the technical merits of the position.

Recently Issued Accounting Pronouncements

On August 26, 2016, the FASB issued Accounting Standards Update, or ASU, 2016-15, *Statement of Cash Flows* (Topic 230). This update affects all entities that are required to present a statement of cash flows and provides guidance and clarity on certain cash flow classification aspects. This update addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice. The ASU is effective for public companies for fiscal years beginning after December 15, 2017 and interim periods within those fiscal years, and early adoption is permitted. We are currently evaluating the impact, if any, of adopting this guidance on our financial statements.

In March 2016, the FASB issued ASU 2016-09, *Compensation Stock Compensation: Improvements to Employee Share-Based Payment Accounting*, which amended previous guidance on employee share-based payment accounting. This update involves several aspects of the accounting for share-based payment transactions, including income tax effects, forfeitures and classifications on the statement of cash flows. This guidance is effective for the Company s fiscal year beginning January 1, 2017. We do not believe that adoption of this guidance will have a material impact on our financial position or results of operations.

In February 2016, the FASB issued ASU 2016-02, *Leases*, which is intended to increase the transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet and disclosing key information about leasing arrangements. In order to meet that objective, the new standard requires recognition of the assets and liabilities that arise from leases. A lessee will be required to recognize on the balance sheet the assets and liabilities for leases with lease terms of more than 12 months. The new standard is effective for public companies for our fiscal year beginning January 1, 2019, and early adoption is permitted. We are currently evaluating the potential impact of this guidance on our financial statements and related financial statement disclosures.

In January 2016, the FASB issued ASU 2016-01, *Financial Instruments: Recognition and Measurement of Financial Assets and Financial Liabilities*. This update addresses certain aspects of the recognition, measurement, presentation,

and disclosure of financial instruments. The new standard is effective for the Company s fiscal year beginning January 1, 2018. We are currently evaluating the potential impact of this guidance on our financial statements and related financial statement disclosures.

Emerging Growth Company Status

The JOBS Act establishes a class of company called an emerging growth company, which generally is a company whose initial public offering was completed after December 8, 2011 and had total annual gross revenues of less than $1 billion during its most recently completed fiscal year. We currently qualify as an emerging growth company. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year following the fifth anniversary of the date of the first sale of our common stock pursuant to an effective registration statement under the Securities Act, which was on February 15, 2013; (ii) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under applicable SEC rules. We expect that we will remain an emerging growth company for the foreseeable future, but cannot retain our emerging growth company status indefinitely and will no longer qualify as an emerging growth company on or before December 31, 2018.

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We are eligible to take advantage of certain extended accounting standards and exemptions from various reporting requirements that are not available to public reporting companies that are not emerging growth companies, including without limitation the following:

- An emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected to avail ourselves of this extended transition period and, as a result, we will not be required to adopt new or revised accounting standards on the dates on which adoption of such standards is required for other public reporting companies.

- An emerging growth company is exempt from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor s report providing additional information about the audit and financial statements, commonly known as an auditor discussion and analysis.

- An emerging growth company is not required to hold a nonbinding advisory stockholder vote on executive compensation or any golden parachute payments not previously approved by stockholders.

- An emerging growth company is not required to comply with the requirement of auditor attestation of internal controls over financial reporting, which is required for other public reporting companies by Section 404 of the Sarbanes-Oxley Act of 2002.

- An emerging growth company is eligible for reduced disclosure obligations regarding executive compensation in its periodic and annual reports, including without limitation exemption from the requirement to provide a compensation discussion and analysis describing compensation practices and procedures.

- An emerging growth company is eligible for reduced financial statement disclosure in registration statements, which must include two years of audited financial statements rather than the three years of audited financial statements that are required for other public reporting companies.

We expect that we will take advantage of these reduced disclosure obligations for as long as they are available to us.

Results of Operations

Comparison of Years Ended December 31, 2016 and 2015

The following table summarizes our results of operations for 2016 and 2015, together with the changes in those items in dollars and as a percentage (*in thousands, except percentage changes*):

	Years ended December 31, 2016	2015	Dollar Change	Percentage Change
Operating expenses:				
Research and development	$ 76,926	$ 73,511	$ 3,415	5%
General and administrative	23,758	17,069	6,689	39%
Total operating expenses	100,684	90,580	10,104	11%
Loss from operations	(100,684)	(90,580)	(10,104)	11%
Other income (expense), net	(2,955)	(1,878)	(1,077)	(57)%
Net loss	$ (103,639)	$ (92,458)	$ (11,181)	12%

Research and Development Expense. Research and development, or R&D, expenses increased by $3.4 million during 2016 as compared to 2015, an increase of 5%. During 2015, we incurred total costs of $28.2 million in connection with our acquisition of rights to development programs from Teva and Lilly, consisting of the combined $25.3 million value of our common stock issued and combined upfront payments totaling $2.9 million made to Teva and Lilly in connection with these transactions. Excluding these costs, R&D costs increased by $31.6 million, or 70%, during 2016 as compared to the same period in 2015. This increase was due to the $20.7 million increase in the chemistry, manufacturing, and control and external clinical development costs associated with entrectinib and our other product candidates, and increased facilities costs due to an expansion of our leased facilities space. Additionally, we incurred increased personnel costs, including additional stock compensation costs of $0.9 million, due to an increase in R&D personnel.

General and Administrative Expense. General and administrative expenses increased by $6.7 million during 2016 as compared to 2015, an increase of 39%. The increase in general and administrative expenses was primarily attributable to increases in personnel costs, including additional stock compensation costs of $1.5 million. As noted above, we also incurred higher facilities expenses as well as increased consulting fees, outside services costs and depreciation expense.

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Comparison of Years Ended December 31, 2015 and 2014

The following table summarizes our results of operations for 2015 and 2014, together with the changes in those items in dollars and as a percentage (*in thousands, except percentage changes*):

	Years ended December 31, 2015	2014	Dollar Change	Percentage Change
Operating expenses:				
Research and development	$ 73,511	$ 30,505	$ 43,006	141%
General and administrative	17,069	9,506	7,563	80%
Total operating expenses	90,580	40,011	50,569	126%
Loss from operations	(90,580)	(39,861)	(50,719)	127%
Other income (expense), net	(1,878)	(129)	(1,749)	(1,356)%
Net loss	$ (92,458)	$ (39,990)	$ (52,468)	131%

Research and Development Expense. Research and development expense increased by $43.0 million during 2015 as compared to 2014, an increase of 141%. The majority of the increase was due to costs we incurred in connection with our acquisition of rights to development programs from Teva and Lilly during 2015, including the combined $25.3 million value of our common stock issued and combined upfront payments totaling $2.9 million made to Teva and Lilly in connection with these transactions. The remaining increase in research and development expenses during 2015 was primarily attributable to an increase in activities relating to development of entrectinib and our other product candidates (including the assets acquired from Teva in March 2015), increased personnel expenses, including additional stock compensation costs of $1.9 million, related to hiring and engaging additional employees and consultants to help us advance our product candidates, and facilities related expenses as a result of the expansion of our leased facilities space.

General and Administrative Expense. General and administrative expenses increased by $7.6 million during 2015 as compared to 2014, an increase of 80%. The increase in general and administrative expenses was primarily attributable to increases in personnel costs, including additional stock compensation costs of $1.4 million, and additional investor relations, audit, legal and intellectual property costs.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, and through December 31, 2016, we have raised an aggregate of approximately $352.2 million to fund our operations, of which approximately $57.5 million was received from our issuance and sale of our common stock in an underwritten public offering in May 2016, approximately $30.0 million was received from our issuance and sale of our common stock to Lilly in November 2015, approximately $75.0 million was received from our issuance and sale of our common stock in an underwritten public offering in June 2015, approximately $41.6 million was raised through our issuance and sale of our common stock in a registered direct offering in March 2015, approximately $55.2 million was received from our issuance and sale of our common stock in an underwritten public offering in March 2014, approximately $54.1 million was received from our issuance and sale of our common stock in

two private placements in November 2013, approximately $32.0 million was received from the incurrence of indebtedness under our loan agreement with Silicon Valley Bank, or SVB, and Oxford Finance LLC, or Oxford, and collectively with SVB, the Lenders, and approximately $6.0 million was received from our issuance and sale of our preferred stock. We had also received a small amount of funding from our issuance of common stock to our founders in August and September 2011, and from our issuance of common stock upon the exercise from time to time of stock options.

Public Offerings. In May 2016, June 2015 and March 2014, we issued an aggregate of 19,517,464 shares of our common stock in underwritten public offerings. All of the shares issued in the May 2016 offering were sold at a purchase price per share of $6.25, all of the shares issued in the June 2015 offering were sold at a purchase price per share of $17.50, and all of the shares issued in the March 2014 offering were sold at a purchase price per share of $9.15. The offerings generated aggregate gross proceeds of approximately $187.7 million and aggregate net proceeds, after deducting underwriting discounts and commissions and other offering fees and expenses, of approximately $175.5 million.

Private Placements. In November 2015, we issued and sold 1,500,000 shares of common stock to Lilly at a purchase price per share of $20.00, for aggregate gross and net proceeds of $30.0 million (the costs associated with this transaction being negligible). In November 2013, we entered into securities purchase agreements with accredited investors providing for the issuance and sale to such investors of an aggregate of 9,010,238 shares of our common stock in private placement transactions. All of the shares issued in the November 2013 private placements were sold at a purchase price per share of $6.00, for aggregate gross proceeds of approximately

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$54.1 million and aggregate net proceeds, after deducting placement agent and other offering fees and expenses, of approximately $51.0 million.

Registered Direct Offering. In March 2015, we issued an aggregate of 4,158,750 shares of our common stock in a registered direct offering. The shares issued in the offering were sold at a purchase price per share of $10.00 per share, for aggregate gross proceeds of approximately $41.6 million and aggregate net proceeds, after deducting offering fees and expenses, of approximately $41.4 million.

Loan Agreement with SVB and Oxford. In June 2016, we entered into a loan agreement with the Lenders under which we incurred $32.0 million of indebtedness, substantially all of which was used to repay our then-existing $31.0 million loan with SVB. We have a conditional option to borrow an additional $10.0 million tranche under this loan facility upon satisfaction of certain specified criteria. We are required to pay interest on the outstanding borrowings under this loan agreement at an interest rate equal to the Prime Rate plus 4.35% (8.10% at December 31, 2016). Monthly principal payments of approximately $0.9 million commence in July 2018 and are due through June 2021. Further, the terms of the loan agreement require that we make a final lump-sum payment at loan maturity equal to 5.0% of the principal amount of the loans funded thereunder. We may elect to prepay all amounts owed under either or both of the loan tranches prior to the maturity date, provided that we pay a prepayment fee. The prepayment fee will be equal to 2.0% of the amount prepaid if the prepayment occurs on or prior to June 30, 2017, or 1% of the amount prepaid if the prepayment occurs thereafter. Pursuant to the loan agreement, we are bound by certain affirmative and negative covenants setting forth actions that we must and must not take during the term thereof. Under the loan agreement, we must also maintain the majority of our cash in accounts at SVB. Upon the occurrence of an event of default under the loan agreement, subject to cure periods for certain events of default, all amounts owed by us thereunder shall begin to bear interest at a rate that is 3% higher than the rate that is otherwise applicable and may be declared immediately due and payable to the Lenders. We have granted SVB, as collateral agent for the ratable benefit of the Lenders, a security interest in substantially all of our personal property, rights and assets, other than intellectual property, to secure the payment of all amounts owed to the Lenders under the loan agreement. We have also agreed not to encumber any of our intellectual property without the required lenders prior written consent.

Preferred Stock Financings. We received approximately $6.0 million from the issuance and sale of our Series A and Series B preferred stock prior to the closing of our October 2013 merger. We received approximately $500,000 from our issuance and sale of an aggregate of 833,334 shares of our Series A preferred stock at a price per share of $0.60 to one investor in October 2011 and March 2012. We received approximately $5.5 million from our issuance and sale of an aggregate of 1,835,000 shares of our Series B preferred stock at a price per share of $3.00 to a number of investors in June 2012 and December 2012. On October 31, 2013, prior to the closing of the merger in which we became the wholly owned subsidiary of Parent, all then-outstanding shares of each series of our preferred stock were voluntarily converted by the holders thereof into shares of our common stock.

Cash Flows

The following table provides information regarding our cash flows during 2016, 2015 and 2014 (*in thousands*):

	Year ended December 31,		
	2016	**2015**	**2014**
Net cash used in operating activities	$ (90,110)	$ (50,800)	$ (32,488)
Net cash provided by (used in) investing activities	14,268	(60,971)	(74,329)
Net cash provided by financing activities	53,799	151,808	61,359

Net increase/ (decrease) in cash and cash equivalents	$ (22,043)	$ 40,037	$ (45,458)

Comparison of Years Ended December 31, 2016 and 2015

Net Cash Used in Operating Activities. The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was approximately $90.1 million during the year ended December 31, 2016 compared to approximately $50.8 million during the year ended December 31, 2015. The increase in cash used in operating activities was driven primarily by an increase in activities relating to development of entrectinib and our other product candidates, and higher salaries, benefits and personnel-related costs resulting from higher headcount to support our expanded clinical and non-clinical development activities.

Net Cash Provided by (Used in) Investing Activities. Investing activities represent investment activity associated with our investment securities and, to a lesser extent, the cash outflow associated with purchases of fixed assets. Such activities resulted in a net increase of funds of approximately $14.3 million during fiscal 2016, while our investing activities used net cash of approximately $61.0 million during fiscal 2015.

Net Cash Provided by Financing Activities. Net cash provided by financing activities was approximately $53.8 million during the year ended December 31, 2016 compared to approximately $151.8 million during the year ended December 31, 2015. The cash provided

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by financing activities was primarily the result of funds raised through sales of our common stock in 2016 and 2015 and the net borrowings under our term loan agreement during 2016.

Comparison of Years Ended December 31, 2015 and 2014

Net Cash Used in Operating Activities. The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was approximately $50.8 million during the year ended December 31, 2015 compared to approximately $32.5 million during the year ended December 31, 2014. The increase in cash used in operating activities was driven primarily by an increase in activities relating to development of entrectinib and our other product candidates including the assets acquired from Teva and Lilly.

Net Cash Used in Investing Activities. Net cash used in investing activities was approximately $61.0 million during the year ended December 31, 2015 compared to approximately $74.3 million during the year ended December 31, 2014. The cash used in investing activities was primarily the result of investment activity associated with our available-for-sale securities and, to a lesser extent, purchases of fixed assets.

Net Cash Provided by Financing Activities. Net cash provided by financing activities was approximately $151.8 million during the year ended December 31, 2015 compared to approximately $61.4 million during the year ended December 31, 2014. The cash provided by financing activities during both periods was primarily the result of funds raised through sales of our common stock and the net borrowings under our loan agreement with SVB.

Funding requirements

We expect our expenses to continue to increase in the future in connection with the development of our ongoing entrectinib and other development programs. In addition, if we obtain marketing approval for any of our product candidates in the future, which we anticipate would not occur for several years, if at all, we expect we would then incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborators with whom we may engage.

As of December 31, 2016, we had approximately $133.0 million in cash, cash equivalents and investment securities. We expect that our existing cash, cash equivalents and investment securities will enable us to fund our operations and capital expenditure requirements for at least the next twelve months. We expect to need to obtain additional funding in future periods, however, in order to continue our operations and pursue our business plans. If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, limit, reduce or terminate our research and development programs or future commercialization efforts. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and costs of preclinical development, laboratory testing and clinical trials for our development programs;

- the scope, progress, results and costs of companion diagnostic development for our product candidates;

the achievement of development milestones that trigger payments due to our licensing partners;

the extent to which we acquire or in-license other medicines, biomarkers and/or technologies;

the costs, timing and outcome of regulatory review of our product candidates;

the costs of future commercialization activities, including product sales, marketing, manufacturing and distribution, for any of our product candidates for which we receive marketing approval to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of collaborators with whom we may engage;

revenue, if any, received from commercial sales of our product candidates, should any of our product candidates receive marketing approval;

the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims; and

our ability to establish and maintain development, manufacturing or commercial collaborations on favorable terms, if at all.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve product sales. In addition, our product candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of medicines that we do not expect to be commercially available for many

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years, if at all. Accordingly, we will likely need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all.

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, collaborations, strategic alliances and licensing arrangements. Any or all of those sources of funding may not be available when needed on acceptable terms, or at all. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the ownership interest of existing equity holders will be diluted. Also, the terms of any additional equity securities that may be issued in the future may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing may not be available when needed and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or relationships with third parties when needed or on acceptable terms, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. Failure to obtain adequate financing could eventually adversely affect our ability to operate as a going concern.

Contractual Obligations

Contractual obligations and commitments represent future cash commitments and liabilities under agreements with third parties, including our leases and other contractual obligations.

The following table summarizes our long-term, non-cancellable contractual obligations and commitments as of December 31, 2016:

	Payments Due by Period (*amounts in thousands*)				
	Total	Less Than 1 Year	1 to 3 Years	4 to 5 Years	After 5 Years
Operating and capital leases	$ 25,650	$ 2,719	$ 9,165	$ 9,604	$ 4,162
Repayment of term loan (1)	32,000		16,000	16,000	
Total	$ 57,650	$ 2,719	$ 25,165	$ 25,604	$ 4,162

(1) See Note 6 to the Financial Statements included in this Annual Report on Form 10-K for further discussion of our term loan.

We enter into contracts in the normal course of business with clinical sites for the conduct of clinical trials, CROs for preclinical and clinical research studies, professional consultants for expert advice and other vendors for clinical supply manufacturing or other services. These contracts generally provide for termination on notice, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments. Total contractual obligations exclude potential contingent consideration payments pursuant to our license agreements. See Note 8 to the Financial Statements included in this Annual Report on Form 10-K for further discussion of our contingent license obligations. Amounts disclosed in Note 8 to the Financial Statements as contingent or milestone-based obligations

depend on the occurrence of contingent events or the achievement of the milestones and depend greatly on assumptions regarding the likelihood and timing of the events or milestones.

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 under applicable SEC rules.

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

Interest Rate Fluctuation Risk

Some of the securities that we invest in have market risk in that a change in prevailing interest rates may cause the principal amount of the marketable securities to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. We invest our excess cash primarily in commercial paper and debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. Treasury. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk. Additionally, we established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity. Because of the short-term maturities of our cash equivalents and marketable investment securities, we do not believe that an increase in market rates would have

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any significant impact on the realized value of our marketable investment securities. If a 1.0% change in interest rates were to have occurred on December 31, 2016, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

We have a loan arrangement with SVB and Oxford under which we have borrowed $32.0 million, which accrues interest at a variable rate of interest equal to the Prime Rate plus 4.35% (8.10% at December 31, 2016). If a 1.0% change in interest rates were to have occurred on December 31, 2016, this change would not have had a material impact on our interest costs over the life of the loan arrangement.

Foreign Currency Exchange Risk

We contract with CROs and investigational sites in several foreign countries, including countries in Eastern and Western Europe and the Asian Pacific. We are therefore subject to fluctuations in foreign currency rates in connection with these agreements. We do not hedge our foreign currency exchange rate risk. To date we have not incurred any material adverse effects from foreign currency changes on these contracts.

Inflation Risk

Inflation generally affects us by increasing our cost of labor and clinical trial costs. We do not believe that inflation has had a material effect on our business, financial condition or results of operations during the years ended December 31, 2016, 2015 or 2014.

Item 8. Financial Statements and Supplementary Data

The financial statements and the reports of our independent registered accounting firms required pursuant to this item are included in Item 15 of this report and are presented beginning on page F-1.

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

None.

Item 9A. Controls and Procedures

Conclusions Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the SEC s rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by Rule 13a-15(b) under the Exchange Act, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as of the end of the period covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of December 31, 2016 at the reasonable assurance level.

Management s Annual Report on Internal Control over Financial Reporting

Internal control over financial reporting refers to the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with United States generally accepted accounting principles. Internal control over financial reporting includes those policies and procedures that: (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles in the United States, and that our receipts and expenditures are being made in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject

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to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk.

Management is responsible for establishing and maintaining adequate internal control over our financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting. Management has used the framework set forth in the report entitled Internal Control Integrated Framework (2013) published by the Committee of Sponsoring Organizations of the Treadway Commission to evaluate the effectiveness of our internal control over financial reporting. Based on its evaluation, management has concluded that our internal control over financial reporting was effective as of December 31, 2016, the end of our most recent fiscal year.

Pursuant to Regulation S-K 308(b), this Annual Report on Form 10-K does not include an attestation report of our company s registered public accounting firm regarding internal control over financial reporting.

Except for the development and implementation of new policies and procedures regarding our internal control over financial reporting in connection with our growth, there have been no changes in our internal control over financial reporting during our most recent fiscal year that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance

Board of Directors

At February 28, 2017, our board of directors consisted of the following members:

Name	Age	Present Position with Ignyta, Inc.
Jonathan E. Lim, M.D.	45	President, Chief Executive Officer and Chairman of the Board
James Bristol, Ph.D.	70	Director
Alexander Casdin	49	Director, Chairman of Audit Committee
Heinrich Dreismann, Ph.D.	63	Director, Chairman of Compensation Committee
James Freddo, M.D.	62	Director, Chairman of Nominating and Corporate Governance Committee
Steven Hoerter	46	Director

Jonathan E. Lim, M.D. Dr. Lim is a co-founder of Ignyta and joined us as Chairman at our inception in August 2011 and as President and Chief Executive Officer in July 2012. Dr. Lim is also a member of the Board of Visitors of the Moores Cancer Center at the University of California, San Diego, a position he has held since December 2015. Prior to joining Ignyta, Dr. Lim most recently served as Chairman and Chief Executive Officer of Eclipse Therapeutics, Inc., a private biotechnology company discovering and developing monoclonal antibody therapeutics targeting cancer stem cells that he co-founded in March 2011 as a spinout from Biogen Idec and that was sold to Bionomics Ltd., an Australian public biotechnology company discovering and developing drugs targeting oncology and central nervous system disorders, in September 2012. Dr. Lim served as a member of the board of directors of Bionomics Ltd. until November 2015. Prior to founding Eclipse Therapeutics, Dr. Lim served as the President, Chief Executive Officer and a Director of Halozyme Therapeutics, Inc., a public biotechnology company, from May 2003 to December 2010. Prior to that, Dr. Lim s experience included management consulting at McKinsey & Company, a National Institutes of Health Postdoctoral Fellowship at Harvard Medical School and the Dana Farber Cancer Institute, and two years of general surgery residency at New York Hospital-Cornell and Memorial Sloan Kettering Cancer Center. Dr. Lim has B.S. and M.S. degrees from Stanford University, an M.D. from McGill University and an M.P.H. from Harvard University. We believe that Dr. Lim adds value to our board of directors based on his intimate knowledge of our business plans and strategies as a co-founder of our company and his extensive experience as an executive officer and director of multiple public and private biotechnology companies.

James Bristol, Ph.D. Dr. Bristol joined our board of directors in February 2014. Dr. Bristol worked for 33 years in drug discovery research and pre-clinical development at Schering-Plough, Parke-Davis and Pfizer, serving in various senior research and development roles. From 2003 until his retirement in 2007, Dr. Bristol was Senior Vice President of Worldwide Drug Discovery Research at Pfizer Global Research & Development. Dr. Bristol has been a Co-Chairman of the Board of Managers at Deciphera Pharmaceuticals, LLC since 2007 and serves as a Member of the Managing Board. He has also served as a Director of Mnemosyne Pharmaceuticals, Inc. since 2011. In 2009, Dr. Bristol joined Frazier Healthcare Ventures as a Senior Advisor. Dr. Bristol is the author of over 100 publications, abstracts and patents. He conducted postdoctoral research at the University of Michigan (N.I.H. Postdoctoral Fellow) and at The Squibb Institute for Medical Research. Dr. Bristol holds a Ph.D. in organic chemistry from the University of New Hampshire and a B.S. in Chemistry from Bates College. We believe that Dr. Bristol adds value to our board of directors based on his experience in the biopharmaceutical industry, including in management and as a director, as

well as his expertise in drug discovery and development.

Alexander Casdin. Mr. Casdin joined our board of directors in October 2013. Alex Casdin is CEO and Portfolio Manager at Reneo Capital Management L.P., a position he has held since January 2015. From September 2012 through December 2014, Mr. Casdin was a private investor focused on the healthcare sector. From October 2011 through September 2012, Mr. Casdin was the Chief Financial Officer of Sophiris Bio, Corp., a Canadian public urology company. Prior to Sophiris Bio, Mr. Casdin served as the Vice President, Finance of Amylin Pharmaceuticals, a biopharmaceutical company that was acquired by Bristol-Myers Squibb in 2012, a position he held from October 2009 to October 2011. Prior to his position at Amylin Pharmaceuticals, Mr. Casdin founded and operated Casdin Advisors LLC, where he served as a strategic advisor to companies in the life sciences industry. Before founding Casdin Advisors, Mr. Casdin was the Chief Executive Officer and Portfolio Manager of Cooper Hill Partners, LLC, a healthcare investment fund. Mr. Casdin has also held previous positions at Pequot Capital Management and Dreyfus Corporation. Mr. Casdin currently serves on the board of directors of DiaVacs, a private clinical-stage biotechnology company focused on a treatment for Type 1 Diabetes, and the Conquer Cancer Foundation of the American Society of Clinical Oncology, as well as a member of the advisory boards of the Hassenfeld Center For Cancer & Blood Disorders and the Social Enterprise Program of the Columbia Business School, each of which are non-profit entities. He also served on the board of directors of DUSA Pharmaceuticals, a specialty pharmaceutical company in the field of dermatology that was previously listed on the NASDAQ Stock Market and was acquired by Sun Pharmaceutical Industries

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Limited in December 2012, from January 2009 until December 2012. Mr. Casdin earned his B.A. degree from Brown University and his M.B.A., Beta Gamma Sigma, from Columbia Business School. We believe that Mr. Casdin adds value to our board of directors based on his experience with financing and other aspects of company-building for enterprises in our industry.

Heinrich Dreismann, Ph.D. Dr. Dreismann joined our board of directors in October 2013. Dr. Dreismann currently serves on the boards of directors of several public and private diagnostic companies, including Myriad Genetics, Inc., a public molecular diagnostic company, and GeneNews, a Canadian public molecular diagnostics company. Dr. Dreismann also served on the board of directors of Shrink Nanotechnologies, Inc., a nanotechnology company, from June 2009 until November 2011, and Med BioGene, Inc., a Canadian public life sciences company focused on genomic-based clinical laboratory diagnostic tests, from 2008 through 2014. Dr. Dreismann completed a career at Roche Molecular Systems in 2006, where he served since 1985 and held several senior positions, including President and Chief Executive Officer of Roche Molecular Systems, Head of Global Business Development at Roche Diagnostics and Member of Roche s Global Diagnostic Executive Committee. Dr. Dreismann earned a Master of Science in biology and a Doctor of Philosophy in microbiology/molecular biology from Westfaelische Wilhelms University in Muenster, Germany. He conducted his Post-Doctoral studies in microbial genetics at the Centre d Etudes Nucleaires de Saclay, France. We believe that Dr. Dreismann adds value to our board of directors based on his experience as a member of boards of directors and senior management of public companies and his expertise in the molecular diagnostics field.

James Freddo, M.D. Dr. Freddo joined our board of directors in February 2014. Previously, Dr. Freddo was a consultant to Ignyta from July 2013 to February 2014, holding the position of Chief Medical Officer. Prior to joining Ignyta, he served as a consultant from April 2012 until May 2012 and as the Executive Vice President, Clinical Development and Chief Medical Officer from June 2012 until May 2013, in each case for Ruga Corporation, a private oncology biopharmaceutical company. Prior to that, he was the Chief Medical Officer and Senior Vice President, Drug Development at Anadys Pharmaceuticals, a drug development company focused on small molecule therapeutics that was previously listed on the NASDAQ Stock Market and was acquired by Roche in 2011, from July 2006 until March 2012, where he also served as a member of the board of directors from January 2011 until November 2011. Prior to joining Anadys Pharmaceuticals, Dr. Freddo served at Pfizer, a global research-based pharmaceutical company, in La Jolla, California from June 2002 until July 2006, holding the positions of Vice President, Clinical Site Head and Development Site Head and, prior to that, Executive Director and leader of Oncology Clinical Development. Prior to joining Pfizer, Dr. Freddo held a variety of senior management positions at Wyeth-Ayerst Research from 1996 to 2002, in the Oncology, Infectious Diseases and Transplantation Immunology therapeutic areas. He also served as a member of the board of directors for InfuSystems, Inc., a public healthcare products and services company, from 2008 until 2011. Dr. Freddo received an M.D. degree from the University of North Carolina, Chapel Hill, completed his residency training at University of California, San Diego and returned to Chapel Hill for his fellowship training in gynecologic oncology. We believe that Dr. Freddo adds value to our board of directors based on his experience as a member of boards of directors and senior management of life sciences companies and his expertise in drug development, clinical investigations and other aspects of our industry.

Steven Hoerter. Steve Hoerter joined our board of directors in December 2016. Mr. Hoerter currently serves as Chief Commercial Officer of Agios Pharmaceuticals, Inc., a position he has held since February 2016, and has more than twenty years of global pharmaceutical and biotechnology experience, previously having served as executive vice president and chief commercial officer at Clovis Oncology, Inc. There, Mr. Hoerter built and led the global commercial organization that developed go-to-market strategies for two oncology therapies. Before joining Clovis in 2011, he was general manager and management center head at Roche for the Sub-Saharan Africa and Indian Ocean Region. From 2005 to 2010, Mr. Hoerter held a variety of positions at Genentech, Inc., including serving on the senior leadership team for Genentech s BioOncology business as senior director, Pipeline Development and Commercial

Operations. Prior to that, Mr. Hoerter held commercial roles at Chiron Corporation and Eli Lilly and Company in the U.S., Europe and Africa. Mr. Hoerter received a B.A. in Russian and political science from Bucknell University, an M.B.A. from Tilburg University, and an M.S. in management from Purdue University. We believe that Mr. Hoerter adds value to our board of directors based on his senior management experience in the pharmaceutical and biotechnology industry, with expertise in drug development and commercialization, and other aspects of our industry.

Board Independence

Our board of directors has determined that all of our directors are independent directors within the meaning of the applicable NASDAQ Stock Market LLC, or Nasdaq, listing standards, except for Jonathan E. Lim, our President and Chief Executive Officer.

Board Leadership Structure

The board believes that Dr. Lim s service as both chairman of the board and Chief Executive Officer is in the best interest of the company and its stockholders. Dr. Lim possesses detailed and in-depth knowledge of the issues, opportunities and challenges facing the company and its businesses and is thus best positioned to develop agendas that ensure that the board s time and attention are focused on the most critical matters.

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Although we believe that the combination of the chairman and Chief Executive Officer roles is appropriate at this time based upon the current circumstances, our Corporate Governance Guidelines do not establish this approach as a policy. Pursuant to our Corporate Governance Guidelines, the board determines the best board leadership structure for our company from time to time. As part of our annual board self-evaluation process, we evaluate our leadership structure to ensure that the board continues to believe that it provides the optimal structure for our company and stockholders. We recognize that different board leadership structures may be appropriate for companies in different situations. We believe our current leadership structure is the optimal structure for our company at this time.

Dr. Lim s combined role enables decisive leadership, ensures clear accountability, and enhances our ability to communicate our message and strategy clearly and consistently to our stockholders, partners and suppliers, particularly during times of turbulent economic and industry conditions. This is expected to be particularly beneficial in driving a unified approach to core operating processes as we experience significant growth.

Each of the directors other than Dr. Lim is independent, and the board believes that the independent directors provide effective oversight of management. Moreover, in addition to feedback provided during the course of board meetings, the independent directors have regular executive sessions. Following an executive session of independent directors, the independent directors communicate with Dr. Lim directly regarding any specific feedback or issues, provide Dr. Lim with input regarding agenda items for board and board committee meetings, and coordinate with Dr. Lim regarding information to be provided to the independent directors in performing their duties. The board believes that this approach appropriately and effectively complements the combined Chief Executive Officer/chairman structure.

The Board s Role in Risk Oversight

The responsibility for day-to-day risk management lies with our management; however, our board of directors is responsible for risk oversight as part of its fiduciary duty of care to effectively monitor our business operations. Our audit committee, pursuant to its charter, is primarily responsible for overseeing the company s risk management processes on behalf of the full board. The audit committee receives reports from management at least quarterly regarding the company s assessment of risks. In addition, the audit committee reports regularly to the full board of directors, which also considers the company s risk profile. The audit committee and the full board of directors focus on the most significant risks facing the company s business and the company s general risk management strategy, and also ensure that risks undertaken by the company are consistent with the board s appetite for risk. We believe this division of responsibilities is the most effective approach for addressing the risks facing our company and that our board leadership structure supports this approach.

Audit Committee

The audit committee of our board of directors currently consists of Mr. Casdin, Dr. Dreismann and Dr. Freddo. Mr. Casdin serves as the chairman of the committee. The audit committee was established in February 2014. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and the NASDAQ Capital Market. Our board of directors has determined that Mr. Casdin is an audit committee financial expert as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable Nasdaq rules and regulations. The audit committee is governed by a written charter adopted by our board of directors. The audit committee s main function is to oversee our accounting and financial reporting processes and the audits of our financial statements. This committee s responsibilities include, among other things:

appointing our independent registered public accounting firm;

evaluating the qualifications, independence and performance of our independent registered public accounting firm;

approving the audit and non-audit services to be performed by our independent registered public accounting firm;

reviewing the design, implementation, adequacy and effectiveness of our internal accounting controls and our critical accounting policies;

discussing with management and the independent registered public accounting firm the results of our annual audit and the review of our quarterly unaudited financial statements;

reviewing, overseeing and monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to financial statements or accounting matters;

reviewing on a periodic basis, or as appropriate, our investment policy and recommending to our board any changes to such investment policy;

reviewing with management and our auditors any earnings announcements and other public announcements regarding our results of operations;

preparing the report that the SEC requires in our annual proxy statement;

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reviewing and approving any related party transactions and reviewing and monitoring compliance with our code of conduct and ethics; and

reviewing and evaluating, at least annually, the performance of the audit committee and its members including compliance of the audit committee with its charter.

Director Nomination Process

Director Qualifications

The goal of the nominating and corporate governance committee of the Board is to assemble a board of directors that brings to our company a variety of perspectives and skills derived from high quality business and professional experience. In evaluating director nominees, the nominating and corporate governance committee considers the following factors:

personal and professional integrity, ethics and values;

experience in corporate management, such as serving as an officer or former officer of a publicly held company;

strong finance experience;

experience relevant to our industry and with relevant social policy concerns;

experience as a board member of another publicly held company;

relevant academic expertise or other proficiency in an area of our operations, such as clinical, medical or commercial experience in the pharmaceutical and/or companion diagnostics areas;

diversity of expertise and experience in substantive matters pertaining to our business relative to other board members;

diversity of background and perspective, including, but not limited to, with respect to age, gender, race, place of residence and specialized experience;

practical and mature business judgment, including, but not limited to, the ability to make independent analytical inquiries; and

any other relevant qualifications, attributes or skills.

Other than the foregoing, there are no stated minimum criteria for director nominees, although the nominating and corporate governance committee may also consider such other factors as it may deem to be in the best interests of our company and our stockholders. The nominating and corporate governance committee does, however, believe it appropriate for at least one, and preferably, several, members of our board of directors to meet the criteria for an audit committee financial expert as defined by SEC rules, and that a majority of the members of our board of directors meet the definition of independent director under Nasdaq qualification standards. The nominating and corporate governance committee also believes it appropriate for our President and Chief Executive Officer to serve as a member of our board of directors.

Identification and Evaluation of Nominees for Directors

The nominating and corporate governance committee identifies nominees for director by first evaluating the current members of our board of directors willing to continue in service. Current members with qualifications and skills that are consistent with the nominating and corporate governance committee s criteria for board service and who are willing to continue in service are considered for re-nomination, balancing the value of continuity of service by existing members of our board of directors with that of obtaining a new perspective.

If any member of our board of directors does not wish to continue in service, if our board of directors decides not to re-nominate a member for re-election or if the board of directors decides to expand the size of the board, the nominating and corporate governance committee identifies the desired skills and experience of a new nominee in light of the criteria above. The nominating and corporate governance committee generally polls our board of directors and members of management for their recommendations. The nominating and corporate governance committee may also review the composition and qualification of the boards of directors of our competitors, and may seek input from industry experts or analysts. The nominating and corporate governance committee reviews the qualifications, experience and background of the candidates. In making its determinations, the nominating and corporate governance committee evaluates each individual in the context of our board of directors as a whole, with the objective of assembling a group that can best perpetuate the success of our company and represent stockholder interests through the exercise of sound business judgment. After review and deliberation of all feedback and data, the nominating and corporate governance committee makes its recommendation to our board of directors. Historically, the nominating and corporate governance committee has not relied on third-party search firms to identify director candidates. The nominating and corporate governance committee may in the future choose to do so in those situations where particular qualifications are required or where existing contacts are not sufficient to identify an appropriate candidate.

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We have not received director candidate recommendations from our stockholders, and we do not have a formal policy regarding consideration of such recommendations. However, any recommendations received from stockholders will be evaluated in the same manner that potential nominees suggested by board members, management or other parties are evaluated.

Section 16(a) Beneficial Ownership Reporting Compliance

Under Section 16(a) of the Exchange Act, directors, officers and beneficial owners of 10% or more of our common stock are required to file with the SEC on a timely basis initial reports of beneficial ownership and reports of changes regarding their beneficial ownership of our common stock. Officers, directors and 10% beneficial owners are required by SEC regulations to furnish us with copies of all Section 16(a) forms that they file.

Based solely on our review of the copies of such forms received and the written representations from certain reporting persons, we have determined that no officer, director or 10% beneficial owner, or any other person subject to Section 16(a) of the Exchange Act, known to us was delinquent with respect to their reporting obligations as set forth in Section 16(a) of the Exchange Act during the fiscal year ended December 31, 2016.

Code of Ethics

We have adopted a Code of Business Conduct and Ethics that applies to our officers, directors and employees which is available on our internet website at www.ignyta.com. The Code of Business Conduct and Ethics contains general guidelines for conducting the business of our company consistent with the highest standards of business ethics, and is intended to qualify as a code of ethics within the meaning of Section 406 of the Sarbanes-Oxley Act of 2002 and Item 406 of Regulation S-K. In addition, we intend to promptly disclose on our website in the future (i) the nature of any amendment to our Code of Business Conduct and Ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller or persons performing similar functions, and (ii) the nature of any waiver, including an implicit waiver, from a provision of our Code of Business Conduct and Ethics that is granted to one of these specified officers, the name of such person who is granted the waiver and the date of the waiver.

Executive Officers

The table below sets forth the name, age and position of each of our executive officers as of February 28, 2017.

Name	Age	Position
Executive Officers:		
Jonathan E. Lim, M.D.	45	President, Chief Executive Officer and Chairman of the Board
Zachary Hornby	38	Chief Operating Officer
Jacob Chacko, M.D.	38	Chief Financial Officer
Christian V. Kuhlen, M.D.	44	General Counsel and Secretary
William McCarthy	45	Chief Business Officer
Pratik Multani, M.D.	50	Chief Medical Officer
Valerie Harding Start, Ph.D.	57	Senior Vice President, Chemistry, Manufacturing, and Controls

Business Experience

The following is a brief account of the education and business experience of our current executive officers:

The biography of Jonathan E. Lim, M.D., can be found under Directors, Executive Officers and Corporate Governance Board of Directors.

Zachary Hornby. Mr. Hornby joined us in August 2012 as Vice President, Corporate Development, was appointed as our Chief Financial Officer in August 2013, and was appointed Chief Operating Officer in May 2014. Prior to joining Ignyta, Mr. Hornby served as senior director of business development at Fate Therapeutics from August 2010 to August 2012. Prior to Fate Therapeutics, Mr. Hornby was director of business development at Halozyme Therapeutics from January 2008 to August 2010. Prior to Halozyme Therapeutics, Mr. Hornby was senior product manager at Neurocrine Biosciences from June 2006 to January 2008. Prior to Neurocrine Biosciences, Mr. Hornby served as a life sciences consultant at L.E.K. Consulting and in regulatory affairs and business development roles at Transkaryotic Therapies (acquired by Shire Pharmaceuticals in 2005). Mr. Hornby is a director of Independa, Inc. Mr. Hornby holds B.S. and M.S. degrees in biology from Stanford University and an M.B.A. from Harvard Business School.

Jacob Chacko, M.D. Dr. Chacko joined us in May 2014 as Chief Financial Officer. Prior to joining Ignyta, Dr. Chacko was Vice President at TPG Capital from August 2008 to May 2014. Prior to TPG, Dr. Chacko concurrently received his M.D. from UCLA and his M.B.A. from Harvard University. Previously, Dr. Chacko was an Associate serving healthcare clients at the management

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consulting firm McKinsey & Company. He served on the boards of directors of RentPath and EnvisionRx, was an advisor to the Audit Committee of Par Pharmaceutical, and was a board observer to IMS Health and Quintiles Transnational. Dr. Chacko received an M.Sc. in economic and social history from Oxford University, where he was a Marshall Scholar, and a B.A. in biology, B.S. in gerontology, and minor in health policy and management from the University of Southern California.

Christian V. Kuhlen, M.D. Dr. Kuhlen joined Ignyta in July 2016. Prior to joining Ignyta, Dr. Kuhlen was Vice President, General Counsel and Secretary at Genoptix, Inc. (a Novartis company), a role he served in since 2007. At Genoptix, Dr. Kuhlen was responsible for all legal and corporate governance functions, including guiding the company through its initial public offering and follow-on offerings and subsequent sale to Novartis. Prior to Genoptix, Dr. Kuhlen was an attorney with Cooley LLP focusing on the needs of public and private biotechnology companies, including financings, M&A, IP, licensing and corporate governance matters. Prior to medical school, he was a research assistant at The Scripps Research Institute in La Jolla, California. Dr. Kuhlen holds a B.S. in biochemistry and cell biology and a B.A. in economics from UC San Diego, and a J.D. and M.D. from the University of Southern California.

William McCarthy. Mr. McCarthy joined us in December 2015 as Chief Business Officer. Prior to joining Ignyta, from April 2014 to November 2015, Mr. McCarthy was Vice President, Corporate and Business Development at Foundation Medicine, Inc. Prior to Foundation Medicine, Mr. McCarthy held positions of increasing responsibility at Halozyme Therapeutics from 2007 to 2014, including Executive Director, Business Development and Senior Director, Marketing and New Product Planning. From 2006 to 2007, Mr. McCarthy was Associate Director, Finance and Business Planning at Biogen Idec, and from 2005 to 2006, he was Associate Director, New Product Planning at Neurocrine Biosciences. Prior to Neurocrine, Mr. McCarthy spent ten years as a management consultant at IMS Consulting Group, Deloitte Consulting and Cambridge Pharma Consultancy. Mr. McCarthy holds an M.B.A. from London Business School and a B.A. in economics from the University of Exeter.

Pratik Multani, M.D. Dr. Multani joined us in February 2015 as Chief Medical Officer. Prior to joining Ignyta, Dr. Multani was Chief Medical Officer at Fate Therapeutics, Inc., where he served from April 2009 to January 2015. Prior to that, Dr. Multani was Vice President of Clinical Development at Kalypsys, Inc. from 2007 to March 2009. From 2005 to 2007, he served as Senior Vice President of Clinical Development and then Chief Medical Officer at Kanisa Pharmaceuticals, Inc. From 1999 to 2004, Dr. Multani advanced from Associate Director of Oncology and Hematology to Senior Director of Medical Research at Biogen-Idec. Dr. Multani holds an M.S. in epidemiology from Harvard School of Public Health, an M.D. from Harvard Medical School and a B.S. in chemistry and biology from Yale University. He completed his Internal Medicine residency at the Massachusetts General Hospital, followed by a medical oncology fellowship at the Dana Farber/Partners joint program, after which he was a member of the transplant unit at Massachusetts General Hospital.

Valerie Harding Start, Ph.D. Dr. Harding Start joined us in September 2015 as Senior Vice President, Chemistry, Manufacturing, and Controls. Prior to joining Ignyta, Dr. Harding spent more than 25 years in positions of increasing responsibility at Pfizer, including Vice President, Product Differentiation, Vice President, Drug Product Design and Vice President, Pharmaceutical Development. Prior to Pfizer, Dr. Harding spent three years as a Scientist and Team leader at Boots and Company, preceded by three years as a Tutor and Researcher at the University of Nottingham School of Pharmacy. Dr. Harding holds a Ph.D. in Pharmaceutical Microbiology from the University of Nottingham and a B.S. in Pharmacy from the University of London.

Item 11. Executive Compensation

Summary Compensation Table

The following table summarizes the compensation earned in each of our fiscal years ended December 31, 2016 and 2015 by our named executive officers, which consisted of (i) our principal executive officer, and (ii) our two next most highly compensated executive officers other than our principal executive officer who were serving as executive officers as of December 31, 2016 and whose total compensation exceeded $100,000 during the year ended December 31, 2016.

Name and Principal Position	Year ended December 31,	Salary ($)	Bonus ($)	Stock Awards ($) [1]	Option Awards ($) [2]	Non-Equity Incentive Plan Compensation ($)[3]	All other Compensation ($)[4]	Total ($)
Jonathan E. Lim, M.D.	2016	520,000		861,120		208,000	2,650	1,591,770
	2015	505,083			414,593	351,360		1,271,036
Zachary Hornby	2016	395,000		344,448		126,400	2,650	868,498
Pratik Multani, M.D	2016	395,000		315,744		110,600	2,650	823,994

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(1) Amounts represent the grant date fair value of the restricted stock unit awards granted during the fiscal years presented, determined in accordance with FASB ASC Topic 718. All awards are amortized over the vesting life of the award. For information on the valuation assumptions with respect to certain of the option grants reflected in this table, refer to footnotes 2 and 11 in our financial statements for the fiscal year ended December 31, 2016.

(2) Amounts represent the grant date fair value of the option awards granted during the fiscal years presented, determined in accordance with FASB ASC Topic 718. All awards are amortized over the vesting life of the award. For information on the valuation assumptions with respect to certain of the option grants reflected in this table, refer to footnotes 2 and 11 in our financial statements for the fiscal year ended December 31, 2016.

(3) Each named executive officer is eligible for a performance bonus that is based 100% upon the achievement of certain corporate performance goals and objectives. Bonuses are set based on the executive officer s base salary as of the end of the bonus year and are expected to be paid out in the first quarter of the following year. The target levels for executive bonuses are currently 50% of base salary for our chief executive officer, 40% of base salary for our chief operating officer and 35% of base salary for our other named executive officers. Each year our board of directors sets corporate goals and milestones for the year, which generally relate to factors such as clinical and non-clinical development, business development and finance and operations. The compensation committee determines the level of achievement of the corporate goals following each year. This achievement level is then applied to each named executive officer s target bonus to determine that year s total bonus opportunity, with the potential for the compensation committee to exercise discretion in setting final bonus numbers to account for superior or substandard performance of any individual. For 2016, Dr. Lim s, Mr. Hornby s and Dr. Multani s bonus amount was based on 80% corporate goals achievement and resulted in a bonus percentage equal to 40%, 32% and 28% respectively, of Dr. Lim s, Mr. Hornby s and Dr. Multani s respective annual base salaries in effect during that fiscal year. For 2015, bonus amounts were based on 120% of corporate goals achievement and resulted in a bonus percentage of 72% of Dr. Lim s annual base salary in effect during that fiscal year.

(4) All Other Compensation includes $2,650 in employer 401(k) matching contributions for each of Dr. Lim, Mr. Hornby and Dr. Multani.

Narrative Disclosure to Summary Compensation Table

No Employment Agreements; At Will Employees

We do not have formal employment agreements with our named executive officers or any of our other employees, who all serve as at will employees. None of our executive officers has a formal employment agreement with us, and none of them will have such a formal employment agreement unless and until our board of directors, or a committee thereof, and the applicable executive officer approve the terms of any such agreement. As a result, the amount of each of our executive officers annual base salary, cash or other bonus compensation, equity compensation or any other form of compensation may be modified at any time at the discretion of our board of directors.

Other Elements of Compensation

Employee Benefits and Perquisites

Our named executive officers are eligible to participate in our health and welfare plans to the same extent as all full-time employees generally. We do not provide our named executive officers with any perquisites or other personal benefits.

No Tax Gross-Ups

We have not made gross-up payments to cover our named executive officers personal income taxes that may pertain to any of the compensation paid or provided by our company.

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Change in Control Benefits

Our named executive officers may become entitled to certain benefits or enhanced benefits in connection with a change in control of our company, as described below under Potential Payments upon Termination or Change in Control Severance and Change in Control Severance Plan.

Outstanding Equity Awards at Fiscal Year-End

The table below summarizes the aggregate stock and option awards held by our named executive officers as of December 31, 2016.

	Option Awards [1]				Stock Awards [1]	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares or Units of Stock that have not Vested (#)	Market Value of Shares or Units of Stock that have not Vested ($)
Jonathan E. Lim, M.D.	6,251 [2]	694 [2]	$ 0.60	02/13/2023	72,000 [8]	381,600
	300,000 [3]	100,000 [3]	$ 6.00	12/15/2023		
	47,916 [4]	52,084 [4]	$ 6.58	01/07/2025		
Zachary Hornby	2,083 [5]		$ 0.57	12/09/2022	78,800 [9]	417,640
	1,250 [2]	139 [2]	$ 0.60	02/13/2023		
	40,625 [6]	9,375 [6]	$ 1.02	09/08/2023		
	187,500 [3]	62,500 [3]	$ 6.00	12/15/2023		
	23,000 [4]	25,000 [4]	$ 6.58	01/07/2025		
Pratik S. Multani, M.D.	91,666 [7]	108,334 [7]	$ 6.90	02/16/2025	46,400 [10]	245,920

(1) Information regarding potential acceleration of certain equity awards for the NEOs is provided under the heading Potential Payments Upon Termination or Change in Control below.

(2) The option award has a grant date of February 14, 2013 and vests pursuant to the following schedule: 1/48th of the shares subject to the award vested on February 14, 2013, and 1/48th of the shares subject to the award vest on each monthly anniversary thereafter.

(3) The option award has a grant date of December 16, 2013 and vests pursuant to the following schedule: 25% of the shares subject to the award vested on December 2, 2014, and 1/48th of the shares subject to the award vest on each monthly anniversary thereafter.

(4) The option award has a grant date of January 8, 2015 and vests pursuant to the following schedule: 25% of the shares subject to the award vested on January 8, 2016, and 1/48th of the shares subject to the award vest on each monthly anniversary thereafter.

(5)

The option award has a grant date of December 10, 2012 and vests pursuant to the following schedule: 25% of the shares subject to the award vested on December 10, 2013, and 1/48th of the shares subject to the award vest on each monthly anniversary thereafter.

(6) The option award has a grant date of September 9, 2013 and vests pursuant to the following schedule: 25% of the shares subject to the award vested on September 9, 2014, and 1/48th of the shares subject to the award vest on each monthly anniversary thereafter.

(7) The option award has a grant date of February 17, 2015 and vests pursuant to the following schedule: 25% of the shares subject to the award vested on February 17, 2016, and 1/48th of the shares subject to the award vest on each monthly anniversary thereafter.

(8) Represents an RSU award with a grant date of January 7, 2016, subject to time-based vesting requirements pursuant to which all shares subject the award vest on the fifth anniversary of the date of grant.

(9) Represents (i) 50,000 RSU awards with a grant date of January 8, 2015, subject to time-based vesting requirements pursuant to which all shares subject to the award will vest on the fourth anniversary of the date of grant, and (ii) 28,800 RSU awards with a

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grant date of January 7, 2016, subject to time-based vesting requirements pursuant to which all shares subject to the award will vest on the fifth anniversary of the date of grant.

(10) Represents (i) 20,000 RSU awards with a grant date of February 17, 2015, subject to time-based vesting requirements pursuant to which all shares subject to the award will vest on the fourth anniversary of the date of grant, and (ii) 26,400 RSU awards with a grant date of January 7, 2016, subject to time-based vesting requirements pursuant to which all shares subject to the award will vest on the fifth anniversary of the date of grant.

Potential Payments upon Termination or Change in Control

Except as described below, we do not have any agreements, plans or arrangements that provide for payments or benefits to our named executive officers in connection with the resignation, retirement or other termination, a change in control, or a change in a named executive officer s responsibilities following a change in control.

Severance and Change in Control Severance Plan

We maintain the Ignyta, Inc. 2013 Severance and Change in Control Severance Plan, or the Severance Plan, for the benefit of certain employees of our company or any of our parents or subsidiaries as designated by our board of directors, or our Covered Employees. Our board of directors most recently amended the Severance Plan on January 7, 2016.

Our board of directors adopted the Severance Plan to provide assurances of specified severance benefits to Covered Employees whose employment is subject to involuntarily termination by us other than for Cause (as defined in the Severance Plan) under the circumstances described in the Severance Plan, including, but not limited to, following a Change in Control (as defined in the Severance Plan). The severance benefits each Covered Employee could be entitled to receive under the Severance Plan are determined pursuant to each Covered Employee s classification as a Tier 1 Covered Employee, Tier 2 Covered Employee or Tier 3 Covered Employee. Covered Employees are classified as follows:

Tier 1 Covered Employee means our Chief Executive Officer.

Tier 2 Covered Employee means a C-level employee of our company who has been designated by our board of directors as eligible to participate in the Severance Plan.

Tier 3 Covered Employee means a Vice President-level employee of our company who has been designated by our board of directors as eligible to participate in the Severance Plan.

Pursuant to the Severance Plan, if, at any time before or after the 12-month period beginning on the date of a Change in Control, we (or any of our parents or subsidiaries) terminate a Covered Employee s employment other than for Cause (and other than due to death or Disability (as defined in the Severance Plan)), then the Covered Employee will be entitled to receive the following severance benefits, subject to his or her execution of a release of claims and compliance with certain restrictive covenants, including with respect to non-solicitation and non-disparagement:

Continued payment of Base Pay (as defined in the Severance Plan) for 12 months, nine months or six months following termination in the case of a Tier 1, Tier 2 or Tier 3 Covered Employee, respectively; and

Company-paid COBRA coverage for 12 months, nine months or six months following termination in the case of a Tier 1, Tier 2 or Tier 3 Covered Employee, respectively.

Pursuant to the Severance Plan, if, at any time during a specified period of time prior to a Change in Control or within the 12 month period following a Change in Control, we (or any of our parents or subsidiaries) terminate a Covered Employee s employment other than for Cause (and other than due to death or Disability) or the Covered Employee resigns for Good Reason (as defined in the Severance Plan), then the Covered Employee will be entitled to receive the following severance benefits, subject to his or her execution of a release of claims and compliance with certain restrictive covenants, including with respect to non-solicitation and non-disparagement:

The following aggregate cash amount paid in installments over the following time period:

In the case of a Tier 1 Covered Employee, the sum of 2.0 times annualized Base Pay and 2.0 times Target Bonus (each as defined in the Severance Plan) paid in equal installments over the 24-month period following termination;

In the case of a Tier 2 Covered Employee, the sum of 1.0 times annualized Base Pay and 1.0 times Target Bonus paid in equal installments over the 12-month period following termination; or

In the case of a Tier 3 Covered Employee, the sum of 0.75 times annualized Base Pay and 0.75 times Target Bonus paid in equal installments over the nine-month period following termination.

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Company-paid COBRA coverage for 24 months, 12 months or nine months following termination in the case of a Tier 1, Tier 2 or Tier 3 Covered Employee, respectively.

100% accelerated vesting of the Covered Employee s Equity Compensation Awards (as defined in the Severance Plan).

The severance benefits prescribed by the Severance Plan are subject to a Section 280G better-off cutback provision, which provides that, in the event that the benefits provided to the Covered Employee pursuant to the Severance Plan or otherwise constitute parachute payments with the meaning of Section 280G of the Internal Revenue Code of 1986, as amended, or the Code, the Covered Employee s severance benefits under the Severance Plan will either be delivered in full or reduced to the extent necessary to avoid an excise tax under Section 4999 of the Code, whichever would result in the Covered Employee receiving the largest amount of severance benefits on an after-tax basis.

The Severance Plan will automatically terminate on December 16, 2019 unless otherwise extended by our board of directors.

Equity Compensation Plan Information

The following table summarizes securities available under our equity compensation plans as of December 31, 2016.

	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted average exercise price of outstanding options, warrants and rights	Number of securities available for future issuance under equity compensation plans (excluding securities reflected in the second column)
Equity compensation plans approved by security holders:			
Amended and Restated 2011 Stock Incentive Plan (1)	294,755	$ 2.94	
Amended and Restated 2014 Incentive Award Plan (2)	2,493,364	$ 8.71	3,525,680
Equity compensation plans not approved by security holders:			
Amended and Restated 2011 Stock Incentive Plan (1) (3)	902,917	$ 6.83	
	440,167	$ 7.43	

Employment Inducement Incentive Award Plan (4)			
2015 Employment Inducement Incentive Award Plan (5)	1,216,562	$	12.61

(1) The material features of the Amended and Restated 2011 Stock Incentive Plan are described in footnote 11 to our financial statements for the fiscal year ended December 31, 2015. Effective June 11, 2014, the 2014 Incentive Award Plan replaced the Amended and Restated 2011 Stock Incentive Plan and the Employment Inducement Incentive Award Plan, and our board of directors will not grant any future awards under the Amended and Restated 2011 Stock Incentive Plan or the Employment Inducement Incentive Award Plan.

(2) The material features of the 2014 Incentive Award Plan are described in footnote 11 to our financial statements for the fiscal year ended December 31, 2015.

(3) On December 16, 2013, our board of directors approved an amendment to the Amended and Restated 2011 Stock Incentive Plan to increase the total number of shares of our common stock available for issuance thereunder from 712,652 shares to 2,712,652 shares. That amendment became effective on December 16, 2013 upon the approval thereof by our board of directors; however, our stockholders did not approve such increase to the share reserve. Effective June 11, 2014, the 2014 Incentive Award Plan replaced the Amended and Restated 2011 Stock Incentive Plan and the Employment Inducement Incentive Award Plan, and our board of directors will not grant any future awards under the Amended and Restated 2011 Stock Incentive Plan or the Employment Inducement Incentive Award Plan.

(4) The material features of the Employment Inducement Incentive Award Plan are described in footnote 11 to our financial statements for the fiscal year ended December 31, 2015. Effective June 11, 2014, the 2014 Incentive Award Plan replaced the Amended and Restated 2011 Stock Incentive Plan and the Employment Inducement Incentive Award Plan, and our board of directors will not grant any future awards under the Amended and Restated 2011 Stock Incentive Plan or the Employment Inducement Incentive Award Plan.

(5) The material features of the 2015 Employment Inducement Incentive Award Plan are described in footnote 11 to our financial statements for the fiscal year ended December 31, 2015. Effective June 13, 2016, in connection with the approval of our amended and restated 2014 Incentive Award Plan by our stockholders, our board of directors determined that we will not grant any future awards under the 2015 Employment Inducement Incentive Award Plan.

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Policies Regarding Tax Deductibility of Compensation

Section 162(m) of the Code restricts the ability of publicly held companies to take a federal income tax deduction for compensation paid to certain of their executive officers to the extent that compensation exceeds $1.0 million per covered officer in any fiscal year. However, this limitation does not apply to compensation that is qualified performance-based compensation under Section 162(m) of the Internal Revenue Code. The non-performance based compensation paid in cash to our executive officers for the 2014, 2015 and 2016 fiscal years did not exceed the $1.0 million limit per officer.

While we consider the tax deductibility of each element of executive compensation as a factor in our overall compensation program, the compensation committee retains the discretion to approve compensation that may not qualify for the compensation deduction if, in light of all applicable circumstances, it would be in our best interest for such compensation to be paid without regard to whether it may be tax deductible.

Director Compensation

In December 2013, our board of directors approved a director compensation program applicable to our non-employee directors. That program provided for annual cash compensation of $35,000 for each non-employee member of our board of directors.

On March 10, 2016, our board of directors amended the director compensation program so that this annual compensation amount is $40,000 beginning with the 2016 fiscal year. In addition, our lead independent director, if any, will receive an additional annual cash retainer of $20,000, the chair of our audit committee will receive an additional annual cash retainer of $15,000, the chair of our compensation committee will receive an additional annual cash retainer of $10,000 and the chair of our nominating and corporate governance committee will receive an additional annual cash retainer of $7,500. Audit committee members will receive an additional annual cash retainer of $7,500, compensation committee members will receive an additional annual cash retainer of $5,000 and nominating and corporate governance committee members will receive an additional annual cash retainer of $3,500. Under the March 2016 director compensation program, each of our non-employee directors was eligible to receive an annual grant of options to purchase 15,000 shares of our common stock at each annual meeting of our stockholders, beginning with the 2016 annual meeting, and upon appointment, new non-employee directors were eligible to receive an initial grant of options to purchase 24,000 shares of our common stock. It was anticipated that all such option grants will be granted under the 2014 Plan, or any other equity compensation plan our board of directors and stockholders may approve and adopt in the future.

On March 10, 2016, each of Mr. Casdin and Dr. Dreismann was granted a fully-vested option to purchase 15,000 shares of our common stock under the 2014 Plan.

On December 8, 2016, in connection with his appointment as non-employee director, our board of directors granted to Mr. Hoerter an option to purchase 24,000 shares of our common stock under the 2014 Plan. The options will vest as to one-third of the total number of shares subject to the award on the first anniversary of the date of grant, and the remainder vesting in equal monthly installments over the two years thereafter.

On March 9, 2017, our board of directors further amended the director compensation program. The cash compensation under the amended director compensation program remained unchanged from the cash compensation under the director compensation program adopted in March 2016. However, under the amended director compensation program, each of our non-employee directors will be eligible to receive an annual grant of options to purchase 20,000 shares of our common stock at each annual meeting of our stockholders, beginning with the 2017 annual meeting, and upon

appointment, new non-employee directors was eligible to receive an initial grant of options to purchase 40,000 shares of our common stock. Initial grants will vest over three years, with one-third of the options vesting on the first anniversary of the date of grant and the remainder vesting in equal monthly installments over the two years thereafter. Annual grants will vest on the first to occur of (1) the first anniversary of the date of grant or (2) the next occurring annual meeting of our stockholders. In addition, all of the options granted to the non-employee directors will vest in full immediately prior to the occurrence of a change in control. It is anticipated that all such option grants will be granted under the 2014 Plan, or any other equity compensation plan our board of directors and stockholders may approve and adopt in the future.

Summary of Director Compensation

The table below summarizes all compensation earned by each of our non-employee directors for services performed during our fiscal year ended December 31, 2016. Dr. Lim is not in the table below because he receives no separate compensation for his services as a director of our company; all of the compensation earned by Dr. Lim during our 2016 fiscal year as an executive officer of our company is reflected in the Summary Compensation Table above.

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Name	Fees earned or paid in cash ($)	Option awards ($)[1]	All other compensation ($)	Total ($)
James Bristol, Ph.D.[2]	48,500	55,569		104,069
Alexander Casdin[3]	63,281	120,969		184,250
Heinrich Dreismann, Ph.D.[4]	57,500	120,969		178,469
James Freddo, M.D.[5]	55,000	55,569		110,569
Steven Hoerter [6]	2,609	104,160		106,769

(1) Amounts represent the grant date fair value of the option awards, determined in accordance with FASB ASC Topic 718. All awards are amortized over the vesting life of the award. For information on the valuation assumptions with respect to these option grants, refer to footnotes 2 and 11 in our financial statements for the fiscal year ended December 31, 2016.
(2) As of December 31, 2016, Dr. Bristol held 39,000 outstanding stock options.
(3) As of December 31, 2016, Mr. Casdin held 70,666 outstanding stock options.
(4) As of December 31, 2016, Dr. Dreismann held 70,666 outstanding stock options.
(5) As of December 31, 2016, Dr. Freddo held 50,666 outstanding stock options.
(6) As of December 31, 2016, Mr. Hoerter held 24,000 outstanding stock options.

Compensation Committee Interlocks and Insider Participation

We did not have a compensation committee until February 28, 2014. On that date, Dr. Bristol, Mr. Casdin and Dr. Dreismann were appointed to our compensation committee. None of the members of our compensation committee has ever been one of our officers or employees. None of our executive officers currently serves, or has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

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

The following table sets forth certain information regarding the beneficial ownership of our common stock as of February 28, 2017, by (i) each person who, to our knowledge, owns more than 5% of our common stock, (ii) each of our current directors and the named executive officers identified under the heading Executive Compensation, (iii) certain of our other executive officers that may be named executive officers for the fiscal year ending December 31, 2017, and (iv) all of those directors and executive officers as a group. We have determined beneficial ownership in accordance with applicable rules of the SEC, and the information reflected in the table below is not necessarily indicative of beneficial ownership for any other purpose. Under applicable SEC rules, beneficial ownership includes any shares of common stock as to which a person has sole or shared voting power or investment power and any shares of common stock which the person has the right to acquire within 60 days after February 28, 2017 through the exercise of any option, warrant or right or through the conversion of any convertible security. Unless otherwise indicated in the footnotes to the table below and subject to community property laws where applicable that, we believe, based on the information furnished to us, each of the persons named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned.

The information set forth in the table below is based on 41,700,063 shares of our common stock issued and outstanding on February 28, 2017. In computing the number of shares of common stock beneficially owned by a person and the percentage ownership of that person, we deemed to be outstanding all shares of common stock subject

to options, warrants, rights or other convertible securities held by that person that are currently exercisable or will be exercisable within 60 days after February 28, 2017. We did not deem these shares outstanding, however, for the purpose of computing the percentage ownership of any other person. Except as otherwise noted, the address for each person listed in the table below is c/o Ignyta, Inc., 4545 Towne Centre Court, San Diego, California 92121.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage Beneficially Owned
5% Stockholders:		
Great Point Partners, LLC [1]	4,000,000	9.59%
Tang Capital Partners LP [2]	3,972,800	9.53%
City Hill Venture Partners I, LLC[3]	3,350,000	8.03%
Cephalon, Inc.[4]	3,000,000	7.19%

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Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage Beneficially Owned
Eli Lilly and Company[5]	2,713,000	6.51%
Victory Capital Management Inc. [6]	2,414,093	5.79%
Broadfin Capital, LLC[7]	2,256,546	5.41%
Directors and Executive Officers:		
Jonathan E. Lim, M.D.[8]	3,804,861	9.04%
Zachary Hornby[9]	338,457*	
Jacob Chacko, M.D. [10]	207,696*	
Christian Kuhlen, M.D.	*	
Pratik Multani, M.D. [11]	108,333*	
William McCarthy [12]	66,666*	
Valerie Harding Start [13]	79,166*	
James Bristol, Ph.D.[14].	45,667*	
Alexander Casdin[15]	862,130	2.06%
Heinrich Dreismann, Ph.D.[16]	55,666*	
James Freddo, M.D.[17]	38,110*	
Steve Hoerter	*	
All Directors and Executive Officers as a Group (12 persons) [18]	5,606,752	13.04%

(1) Based on information disclosed in the Schedule 13G filed with the SEC on May 9, 2016 by Great Point Partners, LLC. Represents 1,079,277 shares held by Biomedical Value Fund, L.P., or BVF, 1,555,544 shares held by Biomedical Offshore Value Fund, Ltd., or BOVF, 1,206,025 shares held by GEF-SMA, L.P., or GEF-SMA, and 159,154 shares held by Class D Series of GEF-PS, LP, or GEF-PS. Great Point Partners, LLC is the investment manager of each of BVF, BOVF, GEF-SMA and GEF-PS, and by virtue of such status may be deemed to be the beneficial owner of the shares held by BVF, BOVF, GEF-SMA and GEF-PS. Each of Dr. Jeffrey R. Jay, M.D., as senior managing member of Great Point Partners, LLC, and Mr. David Kroin, as special managing member of Great Point Partners, LLC, has voting and investment power with respect to the shares held by BVF, BOVF, GEF-SMA and GEF-PS and therefore may be deemed to be the beneficial owner of the shares held by BVF, BOVF, GEF-SMA and GEF-PS. The address of Great Point Partners, LLC is 165 Mason Street, 3rd Floor, Greenwich, CT 06830.

(2) Based on information disclosed in the Schedule 13G filed with the SEC on May 9, 2016 by Tang Capital Partners, LP. Tang Capital Partners, LP, Tang Capital Management, LLC and Kevin C. Tang share voting and dispositive power with respect to the shares. Tang Capital Management, LLC is the general partners of Tang Capital Partners, LP and Kevin C. Tang is the manager of Tang Capital Management, LLC. Mr. Tang disclaims beneficial ownership of the shares except to the extent of his pecuniary interest therein. The address of Tang Capital Partners, LP, Tang Capital Management, LLC and Mr. Tang is 4747 Executive Drive, Suite 510, San Diego CA 92121.

(3) Dr. Jonathan E. Lim, our President, Chief Executive Officer and Chairman of our board of directors, is the Manager of City Hill Ventures, LLC, which is the Manager of City Hill Venture Partners I, LLC, and as such he and City Hill Ventures, LLC have the power to vote or dispose of the securities held of record by City Hill Venture Partners I, LLC and may be deemed to beneficially own those securities. Dr. Lim disclaims beneficial ownership of the securities held of record by City Hill Venture Partners I, LLC except to the extent of his

pecuniary interest therein. The address of City Hill Venture Partners I, LLC is 11575 Sorrento Valley Road, Suite 200, San Diego, California 92121.

(4) Based on information disclosed in the Schedule 13G filed with the SEC by Cephalon, Inc., a Delaware corporation, or Cephalon, and Teva Pharmaceutical Industries Limited, an Israel company and parent of Cephalon, or Teva, on March 27, 2015. Teva may be deemed to have sole voting and dispositive power over all of the shares. The address of Cephalon is 1090 Horsham Road, North Wales, PA 19454. The address of Teva is 5 Basel Street, PO Box 3190, Petach Tikva 4951033, Israel.

(5) Based on information disclosed in the Schedule 13G filed with the SEC on November 16, 2015. Eli Lilly and Company has the sole power to dispose or direct the disposition of, and the sole power to vote, all of such shares. The address of Eli Lilly and Company is Lilly Corporate Center, Indianapolis, Indiana 46285.

(6) Based on information disclosed in the Schedule 13G filed with the SEC on February 10, 2017 by Victory Capital Management Inc. The address of Victory Capital Management Inc. is 4900 Tiedeman Road, 4th Floor, Brooklyn, OH 44144.

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(7) Based on information disclosed in the Schedule 13G filed with the SEC on February 13, 2017 by Broadfin Capital, LLC. Broadfin Capital, LLC, Broadfin Healthcare Master Fund, Ltd. and Kevin Kotler share voting and dispositive power with respect to the shares. Mr. Kotler is the Managing Member of Broadfin Capital, LLC and Director of Broadfin Healthcare Master Fund, Ltd. Broadfin Capital, LLC and Mr. Kotler disclaim beneficial ownership of the shares except to the extent of their pecuniary interests therein. The address of Broadfin Capital, LLC and Mr. Kotler is 300 Park Avenue, 25th Floor, New York, New York 10022, and the address of Broadfin Healthcare Master Fund, Ltd. is 20 Genesis Close, Ansbacher House, Second Floor, PO Box 1344, Grand Cayman KY1-1108, Cayman Islands.

(8) Includes (a) 3,350,000 shares of our common stock held by City Hill Venture Partners I, LLC, with respect to which Dr. Lim has sole voting and investment control, (b) 58,333 shares of our common stock held by Dr. Lim and (c) 396,528 shares underlying options held by Dr. Lim and exercisable within 60 days following February 28, 2017.

(9) Includes 283,596 shares underlying options held by Mr. Hornby and exercisable within 60 days following February 28, 2017.

(10) Includes 191,258 shares underlying options held by Dr. Chacko and exercisable within 60 days following February 28, 2017.

(11) Represents 108,333 shares underlying options held by Dr. Multani and exercisable within 60 days following February 28, 2017.

(12) Represents 66,666 shares underlying options held by Mr. William McCarthy within 60 days following February 28, 2017.

(13) Represents 79,166 shares underlying options held by Dr. Valerie Harding Start 60 days following February 28, 2017.

(14) Includes 24,000 shares underlying options held by Dr. Bristol and exercisable within 60 days following February 28, 2017.

(15) Includes 155,666 shares underlying options held by Mr. Casdin and exercisable within 60 days following February 28, 2017. Also includes 706,464 shares held by Reneo Capital SPV I LP. Mr. Casdin is the Managing Member of Reneo GP, LLC, which is the General Partner of Reneo Capital SPV I LP. Mr. Casdin disclaims beneficial ownership of the shares held by Reneo Capital SPV I LP except to the extent of his pecuniary interest therein.

(16) Represents 55,666 shares underlying options held by Dr. Dreismann and exercisable within 60 days following February 28, 2017.

(17) Represents 35,110 shares underlying options held by Dr. Freddo and exercisable within 60 days following February 28, 2017.

(18) Includes 1,295,989 shares underlying options exercisable within 60 days following February 28, 2017.

Equity Compensation Plans

Information about our equity compensation plans is incorporated by reference to Item 11 of Part III of this Annual Report on Form 10-K.

Item 13. Certain Relationships, Related Transactions and Director Independence

Except as described below and except for compensation for employment or services provided in other roles, the following is a description of transactions since January 1, 2016 to which we are or were a party in which the amount involved exceeds $120,000, and in which any of our current directors, executive officers, holders of more than 5% of any class of our voting securities or any of their respective affiliates or immediate family members, had, or will have, a direct or indirect material interest.

We also describe below certain other transactions with our directors, executive officers and stockholders. Pursuant to the written charter of our audit committee, the audit committee is responsible for reviewing and approving all transactions in which we are a participant and in which any parties related to us, including our executive officers, our directors, beneficial owners of more than 5% of our securities, immediate family members of the foregoing persons and any other persons whom our board of directors determines may be considered related parties under Item 404 of Regulation S-K, has or will have a direct or indirect material interest.

Insider Participation in Public Offering

On May 4, 2016, we issued an aggregate of 9,200,000 shares of our common stock in an underwritten public offering at a purchase price per share of $6.25 per share. Reneo Capital SPV I LP purchased 232,000 of these shares, for an aggregate purchase price of $1,450,000. Alexander Casdin, a member of our board of directors, is the Managing Member of Reneo GP, LLC, which is the General Partner of Reneo Capital SPV I LP.

Indemnification of Officers and Directors

Our second amended and restated certificate of incorporation provides for indemnification of our directors and officers substantially identical in scope to that permitted under applicable Delaware law. Our second amended and restated certificate of incorporation also provides that the expenses of our directors and officers incurred in defending any applicable action, suit or proceeding must be paid by

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us as they are incurred and in advance of the final disposition of the action, suit or proceeding, provided that the required undertaking by the director or officer is delivered to us.

We have also entered into separate indemnification agreements with each of our current directors and executive officers consistent with Delaware law and in the form approved by our board of directors and our stockholders, and we contemplate entering into such indemnification agreements with directors and certain executive officers that may be elected or appointed in the future. Those indemnification agreements require that under the circumstances and to the extent provided for therein, we indemnify such persons to the fullest extent permitted by applicable law against certain expenses incurred by any such person as a result of such person being made a party to certain actions, suits and proceedings by reason of the fact that such person is or was a director, officer, employee or agent of our company, any entity that was a predecessor corporation of our company or any of our affiliates. The rights of each person who is a party to such an indemnification agreement are in addition to any other rights such person may have under applicable Delaware law, our second amended and restated certificate of incorporation, our bylaws, any other agreement, any vote of our stockholders, a resolution adopted by our board of directors or otherwise. We also maintain a customary insurance policy that indemnifies our directors and officers against various liabilities, including liabilities arising under the Securities Act, that may be incurred by any director or officer in his or her capacity as such.

Director Independence

Our board of directors has determined that all of our directors are independent directors within the meaning of the applicable Nasdaq listing standards, except for Jonathan Lim, our President and Chief Executive Officer.

Item 14. Principal Accounting Fees and Services

On June 28, 2016, we, at the discretion of our audit committee, dismissed Mayer Hoffman McCann P.C. as our independent registered public accounting firm and appointed KPMG LLP to serve as our independent registered public accounting firm for the fiscal year ended December 31, 2016. We filed a Current Report on Form 8-K on July 1, 2016 reporting this change.

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The following table represents aggregate fees for professional audit services rendered by KPMG LLP and Mayer Hoffman McCann P.C. related to the fiscal years ended December 31, 2016 and 2015, respectively.

	Year Ended December 31,	
	2016	2015
	(KPMG)	(Mayer Hoffman)
Audit Fees[1]	$ 248,175	$ 186,372
Audit Related Fees		
Tax Fees		
All Other Fees		
	$ 248,175	$ 186,372

(1) Audit fees consist of fees and out-of-pocket expenses whether or not yet invoiced for professional services provided in connection with the audit of our annual financial statements, review of our quarterly financial statements, due diligence procedures to support comfort and/or consent letters in connection with our public offerings and the resale registration statements relating to our private placements of common stock, and related services that are normally provided in connection with statutory and regulatory filings or engagements.

Pre-Approval Policies and Procedures

Our audit committee has established a policy that all audit and permissible non-audit services provided by our independent registered public accounting firm will be pre-approved by the audit committee. Prior to February 28, 2014, when our audit committee was formed, our full board of directors had responsibility for the activities that were delegated to the audit committee. All audit and permissible non-audit services were pre-approved by our audit committee or board of directors in accordance with this policy during the fiscal years ended December 31, 2016 and 2015. These services may include audit services, audit-related services, tax services and other services. The audit committee considers whether the provision of each non-audit service is compatible with maintaining the independence of our auditors. Pre-approval is detailed as to the particular service or category of services and is generally subject to a specific budget. Our independent registered public accounting firm and management are required to periodically report to the audit committee regarding the extent of services provided by the independent registered public accounting firm in accordance with this pre-approval, and the fees for the services performed to date.

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PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) Documents filed as part of this report.

1. *Financial Statements.* The following financial statements of Ignyta, Inc., together with the reports thereon of KPMG LLP, and Mayer Hoffman McCann P.C., each an independent registered public accounting firm, are included in this Annual Report on Form 10-K:

2. *Financial Statement Schedules.*

All schedules are omitted because they are not applicable or the required information is shown in the financial statements or notes thereto.

3. *Exhibits.*

A list of exhibits to this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding such exhibits and is incorporated herein by reference.

(b) See Item 15(a)(2) above.

(c) See Item 15(a)(2) above.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

IGNYTA, INC.

Date: March 14, 2017

By: /s/ Jonathan E. Lim, M.D.
Jonathan E. Lim, M.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ Jonathan E. Lim, M.D. Jonathan E. Lim, M.D.	President and Chief Executive Officer and Chairman of the Board (Principal Executive Officer)	March 14, 2017
/s/ Jacob Chacko, M.D. Jacob Chacko, M.D.	Chief Financial Officer (Principal Financial and Accounting Officer)	March 14, 2017
/s/ James Bristol, Ph.D. James Bristol, Ph.D.	Director	March 14, 2017
/s/ Alexander Casdin Alexander Casdin	Director	March 14, 2017
/s/ Heinrich Dreismann, Ph.D. Heinrich Dreismann, Ph.D.	Director	March 14, 2017
/s/ James Freddo, M.D. James Freddo, M.D.	Director	March 14, 2017
/s/ Steven Hoerter Steven Hoerter	Director	March 14, 2017

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EXHIBIT INDEX

Exhibit Number	Description of Exhibit
2.1	Agreement and Plan of Reorganization, dated May 7, 2013, by and between Ignyta, Inc. and Actagene Oncology, Inc. (incorporated by reference to Exhibit 2.1 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
2.2	Agreement and Plan of Merger and Reorganization, dated October 31, 2013, by and among Ignyta, Inc. (then known as Infinity Oil & Gas Company), IGAS Acquisition Corp., and Ignyta, Inc. (then known as Ignyta Operating, Inc.) (incorporated by reference to Exhibit 2.2 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
2.3	Agreement and Plan of Merger, dated June 12, 2014, by and among Ignyta, Inc. (then known as Ignyta Operating, Inc.), and its parent entity Ignyta, Inc. (incorporated by reference to Exhibit 2.1 to the Company s Report on Form 8-K12B filed with the SEC on June 13, 2014).
3.1	Second Amended and Restated Certificate of Incorporation of Ignyta, Inc. (incorporated by reference to Exhibit 3.1 to the Company s Report on Form 8-K12B filed with the SEC on June 13, 2014).
3.2	Amended and Restated Bylaws of Ignyta, Inc. (incorporated by reference to Exhibit 3.2 to the Company s Report on Form 8-K12B filed with the SEC on June 13, 2014).
4.1	Form of Common Stock certificate (incorporated by reference to Exhibit 4.1 to the Company s Report on Form 8-K12B filed with the SEC on June 13, 2014).
4.2	Warrant to Purchase Stock, issued to Silicon Valley Bank on June 25, 2012 (incorporated by reference to Exhibit 10.5 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
4.3	Warrant to Purchase Stock, issued to Silicon Valley Bank on February 27, 2013 (incorporated by reference to Exhibit 10.6 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
4.4	Warrant to Purchase Common Stock, dated November 6, 2013, issued to Nerviano Medical Sciences S.r.l. (incorporated by reference to Exhibit 10.3 to the Company s Current Report on Form 8-K filed with the SEC on November 7, 2013).
4.5	Warrant to Purchase Stock, issued to Silicon Valley Bank on September 30, 2014 (incorporated by reference to Exhibit 4.1 to the Company s Current Report on Form 8-K filed with the SEC on October 1, 2014).
4.6	Warrant to Purchase Stock, issued to Life Science Loans, LLC on September 30, 2014 (incorporated by reference to Exhibit 4.2 to the Company s Current Report on Form 8-K filed with the SEC on October 1, 2014).
4.7	Warrant to Purchase Stock, issued to Silicon Valley Bank on September 30, 2015 (incorporated by reference to Exhibit 4.1 to the Company s Current Report on Form 8-K filed with the SEC on September 30, 2015).
4.8	Warrant to Purchase Stock, issued to Life Science Loans, LLC on September 30, 2015 (incorporated by reference to Exhibit 4.2 to the Company s Current Report on Form 8-K filed with the SEC on September 30, 2015).

4.9	Warrant to Purchase Stock, issued to Silicon Valley Bank on June 30, 2016 (incorporated by reference to Exhibit 4.1 to the Company s Current Report on Form 8-K filed with the SEC on July 1, 2016).
4.10	Warrant to Purchase Stock, issued to Oxford Finance, LLC on June 30, 2016 (incorporated by reference to Exhibit 4.2 to the Company s Current Report on Form 8-K filed with the SEC on July 1, 2016).
4.11	Warrant to Purchase Stock, issued to Oxford Finance, LLC on June 30, 2016 (incorporated by reference to Exhibit 4.3 to the Company s Current Report on Form 8-K filed with the SEC on July 1, 2016).
4.12	Warrant to Purchase Stock, issued to Oxford Finance, LLC on June 30, 2016 (incorporated by reference to Exhibit 4.4 to the Company s Current Report on Form 8-K filed with the SEC on July 1, 2016).
4.13	Warrant to Purchase Stock, issued to Oxford Finance, LLC on June 30, 2016 (incorporated by reference to Exhibit 4.5 to the Company s Current Report on Form 8-K filed with the SEC on July 1, 2016).
10.1#	Ignyta, Inc. Amended and Restated 2011 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
10.2#	Amendment No. 1 to the Ignyta, Inc. Amended and Restated 2011 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Company s Current Report on Form 8-K filed with the SEC on December 19, 2013).

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Exhibit Number	Description of Exhibit
10.3#	Form of Stock Option Award Agreement under the Ignyta, Inc. Amended and Restated 2011 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
10.4#	Form of Restricted Stock Award Agreement under the Ignyta, Inc. Amended and Restated 2011 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
10.5#	Ignyta, Inc. Employment Inducement Incentive Award Plan and form of stock option agreement thereunder (incorporated by reference to Exhibit 10.1 to the Company s Current Report on Form 8-K filed with the SEC on April 1, 2014).
10.6#	Amended and Restated Ignyta, Inc. 2014 Incentive Award Plan (incorporated by reference to Appendix A to the Definitive Proxy Statement on Schedule 14A filed with the SEC on April 29, 2016).
10.7#	Form of Stock Option Agreement under the Ignyta, Inc. 2014 Incentive Award Plan (incorporated by reference to Exhibit 10.3 to the Company s Report on Form 8-K12B filed with the SEC on June 13, 2014).
10.8#	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award under the Ignyta, Inc. 2014 Incentive Award Plan. (incorporated by reference to Exhibit 10.1 to the Company s Quarterly Report on Form 10-Q filed with the SEC on May 11, 2015).
10.9#	Ignyta, Inc. 2015 Employment Inducement Incentive Award Plan and form of stock option agreement thereunder (incorporated by reference to Exhibit 10.1 to the Company s Current Report on Form 8-K filed with the SEC on July 22, 2015).
10.10	License Agreement, dated October 10, 2013, by and between Ignyta, Inc. (then known as Ignyta Operating, Inc.) and Nerviano Medical Sciences, S.r.l., as amended by that certain Amendment No. 1 to License Agreement, dated October 25, 2013, by and between Ignyta, Inc. and Nerviano Medical Sciences, S.r.l. (incorporated by reference to Exhibit 10.4 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013) (portions of this exhibit have been omitted pursuant to a grant of confidential treatment and have been filed separately with the SEC).
10.11	Amendment No. 2 to License Agreement, dated December 12, 2014 by and between Ignyta, Inc. and Nerviano Medical Sciences, S.r.l. (incorporated by reference to Exhibit 10.1 to the Company s Amendment No. 1 to Current Report on Form 8-K filed with the SEC on February 17, 2015) (portions of this exhibit have been omitted pursuant to a grant of confidential treatment and have been filed separately with the SEC),
10.12	Lease, dated February 19, 2013, by and between Ignyta, Inc. and BMR-Coast 9 LP (incorporated by reference to Exhibit 10.9 to the Company s Current Report on Form 8-K filed with the SEC on November 1, 2013).
10.13	Third Amendment to Lease between Ignyta, Inc. and BMR-Coast 9 LP dated April 18, 2014 (incorporated by reference to Exhibit 10.1 to the Company s Current Report on Form 8-K filed with the SEC on April 23, 2014).
10.14	Fifth Amendment to Lease dated October 16, 2015, between Ignyta, Inc. and BMR-Coast 9 LP (incorporated by reference to Exhibit 10.2 to the Company s Current Report on Form 8-K filed with the SEC on October 21, 2015).

10.15	Lease dated October 16, 2015, between Ignyta, Inc. and BMR-Axiom LP (incorporated by reference to Exhibit 10.1 to the Company s Current Report on Form 8-K filed with the SEC on October 21, 2015).
10.16	Asset Purchase Agreement, dated March 17, 2015, by and between Ignyta, Inc. and Cephalon, Inc. (incorporated by reference to Exhibit 10.1 to the Company s Current Report on Form 8-K filed with the SEC on March 17, 2015).
10.17	Registration Rights Agreement, dated March 17, 2015, by and between Ignyta, Inc. and Cephalon, Inc. (incorporated by reference to Exhibit 10.2 to the Company s Current Report on Form 8-K filed with the SEC on March 17, 2015).
10.18	Form of Subscription Agreement dated March 17, 2015 (incorporated by reference to Exhibit 10.1 to the Company s Current Report on Form 8-K filed with the SEC on March 17, 2015).
10.19	Collaboration Agreement dated November 3, 2006, as amended April 17, 2009, by and between Ignyta, Inc., as successor-in-interest to Cephalon, Inc., and Daiichi Sankyo Company Limited, as successor-in-interest to Ambit Biosciences Corporation (incorporated by reference to Exhibit 10.6 to the Company s Quarterly Report on Form 10-Q filed with the SEC on May 11, 2015) (portions of this exhibit have been omitted pursuant to a grant of confidential treatment and have been filed separately with the SEC).

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Exhibit Number	Description of Exhibit
10.20	License, Development and Commercialization Agreement, dated November 6, 2015, by and between the Company and Eli Lilly and Company (incorporated by reference to Exhibit 10.1 to the Company s Registration Statement on Form S-3 filed with the SEC on December 23, 2015) (portions of this exhibit have been omitted pursuant to a grant of confidential treatment and have been filed separately with the SEC).
10.21	Stock Purchase Agreement, dated November 6, 2015, by and between the Company and Eli Lilly and Company (incorporated by reference to Exhibit 10.2 to the Company s Registration Statement on Form S-3 filed with the SEC on December 23, 2015).
10.22	Registration Rights Agreement, dated November 6, 2015, by and between the Company and Eli Lilly and Company (incorporated by reference to Exhibit 10.2 to the Company s Registration Statement on Form S-3 filed with the SEC on December 23, 2015).
10.23	Controlled Equity Offering[SM] Sales Agreement dated as of December 23, 2015 by and between Ignyta, Inc. and Cantor Fitzgerald & Co. (incorporated by reference to Exhibit 10.1 to the Company s Quarterly Report on Form 10-Q filed with the SEC on December 23, 2015).
10.24#	Form of Indemnification Agreement by and between Ignyta, Inc. and each of its current directors and executive officers (incorporated by reference to Exhibit 10.1 to the Company s Report on Form 8-K12B filed with the SEC on June 13, 2014).
10.25#	Amended and Restated Ignyta, Inc. Severance and Change in Control Severance Plan and Summary Plan Description (incorporated by reference to Exhibit 10.1 to the Company s Quarterly Report on Form 10-Q filed with the SEC on May 10, 2016).
10.26	Loan Agreement, dated as of June 30, 2016, between and among Ignyta, Inc., Silicon Valley Bank, as Collateral Agent, and Silicon Valley Bank and Oxford Finance LLC, as Lenders (incorporated by reference to Exhibit 99.1 to the Company s Current Report on Form 8-K filed with the SEC on July 1, 2016).
10.27#*	Non-Employee Director Compensation Program dated March 9, 2017.
23.1*	Consent of independent registered public accounting firm, KPMG LLP
23.2*	Consent of independent registered public accounting firm, Mayer Hoffmann McCann P.C.
31.1*	Certification of Chief Executive Officer pursuant to Rule 13a 14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Chief Financial Officer pursuant to Rule 13a 14(a) and 15d-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18.U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes Oxley Act of 2002.
101.INS*	XBRL Instance Document.
101.SCH*	XBRL Taxonomy Extension Schema Document.
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF*	XBRL Taxonomy Extension Definition Linkbase Document.

101.LAB*	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document.

* Filed herewith.
\# Management contract or compensatory plan or arrangement.

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IGNYTA, INC.

INDEX TO FINANCIAL STATEMENTS

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Report of KPMG LLP,

Independent Registered Public Accounting Firm

The Board of Directors and Stockholders

Ignyta, Inc.:

We have audited the accompanying balance sheet of Ignyta, Inc. as of December 31, 2016, and the related statements of operations and comprehensive loss, stockholders equity, and cash flows for the year ended December 31, 2016. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Ignyta, Inc. as of December 31, 2016, and the results of its operations and its cash flows for the year ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ KPMG LLP

San Diego, California

March 14, 2017

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REPORT OF MAYER HOFFMAN MCCANN P.C.,

INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of Ignyta, Inc.

San Diego, California

We have audited the accompanying balance sheet of Ignyta, Inc. as of December 31, 2015, and the related statements of operations and comprehensive loss, stockholders equity, and cash flows for each of the two years in the period ended December 31, 2015. 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 audit 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 includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes 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, the financial statements referred to above present fairly, in all material respects, the financial position of Ignyta, Inc. as of December 31, 2015, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2015, in conformity with accounting principles generally accepted in the United States of America.

/s/ Mayer Hoffman McCann P.C.

San Diego, CA
March 14, 2016

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Ignyta, Inc.

Balance Sheets

(In thousands, except share data)

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 24,340	$ 46,383
Short-term investment securities	83,637	85,420
Other current assets	3,873	4,191
Total current assets	111,850	135,994
Long-term investment securities	24,983	40,346
Property and equipment, net	6,270	18,764
Other long-term assets	1,811	410
Total assets	$ 144,914	$ 195,514
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable and accrued liabilities	$ 13,510	$ 14,025
Accrued compensation and benefits	4,007	3,844
Current portion of term debt		6,675
Total current liabilities	17,517	24,544
Term debt, net of current portion and discount	29,517	22,821
Other long-term liabilities	3,110	12,164
Total liabilities	50,144	59,529
Commitments and contingencies		
Stockholders equity:		
Preferred stock, $0.0001 par value; 10,000,000 shares authorized; no shares issued or outstanding		
Common stock, $0.0001 par value; 150,000,000 shares authorized; 41,665,779 and 32,339,081 shares issued and outstanding at December 31, 2016 and 2015, respectively	4	3
Additional paid-in capital	346,549	284,252
Accumulated other comprehensive loss	(123)	(249)
Accumulated deficit	(251,660)	(148,021)
Total stockholders equity	94,770	135,985
Total liabilities and stockholders equity	$ 144,914	$ 195,514

See accompanying notes to the financial statements.

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Ignyta, Inc.

Statements of Operations and Comprehensive Loss

(In thousands, except per share data)

	Year ended December 31,		
	2016	**2015**	**2014**
Revenue	$	$	$ 150
Operating expenses:			
Research and development	76,926	73,511	30,505
General and administrative	23,758	17,069	9,506
Total operating expenses	100,684	90,580	40,011
Loss from operations	(100,684)	(90,580)	(39,861)
Other income (expense):			
Interest expense	(3,214)	(2,593)	(1,362)
Interest income and other income/ (expense), net	955	715	1,233
Loss on debt extinguishment	(696)		
Total other income (expense)	(2,955)	(1,878)	(129)
Net loss	$ (103,639)	$ (92,458)	$ (39,990)
Comprehensive loss:			
Net loss	$ (103,639)	$ (92,458)	$ (39,990)
Net unrealized gain (loss) on investment securities	126	(196)	(53)
Comprehensive loss	$ (103,513)	$ (92,654)	$ (40,043)
Net loss per share:			
Net loss per share - basic and diluted	$ (2.69)	$ (3.44)	$ (2.18)
Weighted average shares - basic and diluted	38,480	26,854	18,328

See accompanying notes to the financial statements.

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Ignyta, Inc.

Statements of Stockholders Equity

(In thousands, except share data)

	Common stock		Additional paid-in capital	Accumulated comprehensive loss	Accumulated deficit	Total stockholders equity
	Shares	Amount				
Balance at December 31, 2013	13,934,876	$ 1	$ 57,360	$	$ (15,573)	$ 41,788
Common stock offering, net	6,031,750	1	51,581			51,582
Exercise of stock options	18,143		7			7
Repurchase of unvested restricted stock	(400,000)		(1)			(1)
Reclassification of warrant from liability			125			125
Issuance of warrants to lender			208			208
Stock-based compensation			2,283			2,283
Unrealized loss on investments				(53)		(53)
Net loss					(39,990)	(39,990)
Balance at December 31, 2014	19,584,769	2	111,563	(53)	(55,563)	55,949
Common stock offering, net	9,944,464	1	141,588			141,589
Other issuances of common stock	2,713,000		25,296			25,296
Exercise of stock options	74,529		391			391
Net exercise of warrants	22,319					
Issuance of warrants to lender			69			69
Stock-based compensation			5,345			5,345
Unrealized loss on investments				(196)		(196)
Net loss					(92,458)	(92,458)
Balance at December 31, 2015	32,339,081	3	284,252	(249)	(148,021)	135,985
Common stock offering, net	9,200,000	1	53,891			53,892
Exercise of stock options	126,698		410			410
Issuance of warrants to lender			275			275
Stock-based compensation			7,721			7,721
Unrealized gain on investments				126		126
Net loss					(103,639)	(103,639)
Balance at December 31, 2016	41,665,779	$ 4	$ 346,549	$ (123)	$ (251,660)	$ 94,770

See accompanying notes to the financial statements.

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Ignyta, Inc.

Statements of Cash Flows

(**In thousands**)

	Year ended December 31,		
	2016	**2015**	**2014**
Operating activities:			
Net loss	$ (103,639)	$ (92,458)	$ (39,990)
Adjustments to reconcile net loss to net cash used in operating activities:			
Loss on debt extinguishment	696		
In-process research and development charge associated with asset acquisition		11,880	
Issuance of common stock for technology		13,416	
Stock-based compensation	7,721	5,345	2,283
Depreciation and amortization of property and equipment	3,478	2,037	528
Amortization of premium on investment securities, net of accretion of discounts	688	1,358	887
Amortization of non-cash financing costs	593	538	368
Other	(358)	2	
Change in operating assets and liabilities:			
Prepaid expenses and other assets	(509)	(2,700)	(801)
Accounts payable	95	2,856	164
Accrued expenses and other liabilities	1,125	6,926	4,073
Net cash used in operating activities	(90,110)	(50,800)	(32,488)
Investing activities:			
Purchases of investment securities	(123,857)	(148,111)	(89,286)
Maturities of investment securities	84,755	90,662	18,058
Sales of investment securities	55,746		
Purchases of property and equipment	(2,451)	(3,522)	(3,117)
Proceeds from sale of equipment	75		16
Net cash provided by / (used in) investing activities	14,268	(60,971)	(74,329)
Financing activities:			
Proceeds from issuance of common stock, net of issuance costs	53,892	141,589	51,582
Proceeds from borrowings under term loan facility	17,116	10,000	21,000
Repayments of borrowings under term loan facility	(17,438)		(11,050)
Proceeds from exercise of stock options	410	391	7
Other	(181)	(172)	(180)
Net cash provided by financing activities	53,799	151,808	61,359

Net increase/ (decrease) in cash and cash equivalents	(22,043)	40,037	(45,458)
Cash and cash equivalents at beginning of period	46,383	6,346	51,804
Cash and cash equivalents at end of period	$ 24,340	$ 46,383	$ 6,346
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 2,611	$ 2,528	$ 1,884
Amounts accrued for purchases of property and equipment	$ 357	$	$
Non-cash financing activity:			
Net change in capitalized costs associated with leased building (Note 5)	$ (11,000)	$ 11,000	$
Final loan fee and warrant issuance recorded as debt discount	$ 1,600	$ 369	$ 838
Unrealized gain (loss) on available-for-sale investment securities	$ 126	$ (196)	$ (53)
Leasehold improvements paid by lessor	$	$	$ 2,342
Assets acquired under capital leases	$	$	$ 538
Warrant reclassified to equity due to removal of anti-dilution provision	$	$	$ 125

See accompanying notes to the financial statements.

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Ignyta, Inc.

Notes to Financial Statements

1. ORGANIZATION

Organization and Nature of Operations

Ignyta, Inc. (Ignyta or the Company) is incorporated in the state of Delaware and was founded in 2011 (with the name NexDx, Inc.). The Company changed its name to Ignyta, Inc. on October 8, 2012. Ignyta is a biotechnology company focused on precision medicine in oncology. Its goal is not just to shrink tumors, but to eradicate residual disease the source of cancer relapse and recurrence in precisely defined patient populations. The Company is pursuing an integrated therapeutic (Rx) and companion diagnostic (Dx) strategy for treating patients with cancer. Its Rx efforts are focused on in-licensing or acquiring, then developing and commercializing molecularly targeted therapies that, sequentially or in combination, are foundational for eradicating residual disease. Its Dx efforts aim to pair these product candidates with biomarker-based companion diagnostics that are designed to precisely identify, at the molecular level, the patients who are most likely to benefit from the therapies it develops.

On October 31, 2013, the Company merged with and into IGAS Acquisition Corp., a wholly owned subsidiary of Ignyta, Inc., a Nevada corporation previously named Infinity Oil & Gas Company (Parent), formerly a shell company under applicable rules of the Securities and Exchange Commission (the SEC). The Company changed its name to Ignyta Operating, Inc. in connection with this merger, and it survived the merger as a wholly owned subsidiary of Parent. In the merger, Parent acquired the business of the Company and continued the business operations of the Company. The merger was accounted for as a reverse merger and recapitalization, with the Company as the acquirer and Parent as the acquired company for financial reporting purposes. As a result, the assets and liabilities and the operations that are reflected in the historical financial statements prior to the merger are those of the Company and are recorded at the historical cost basis of the Company, and the financial statements after completion of the merger will include the assets and liabilities of Parent and the Company, the historical operations of the Company and the operations of the combined enterprise of Parent and the Company from and after the closing date of the merger. On June 12, 2014, Parent merged with and into the Company, with the Company surviving the merger and changing its name to Ignyta, Inc. (the Reincorporation Merger). This Reincorporation Merger had no material impact on the accounting of the Company.

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 views its operations and manages its business as one operating segment.

Liquidity

The Company had negative cash flow from operations of approximately $90.1 million during 2016 and, as of December 31, 2016, had an accumulated deficit of approximately $251.7 million. The Company is focused primarily on its development programs, and management believes such activities will result in the continued incurrence of significant research and development and other expenses related to those programs. The Company expects that it will need additional capital to further fund development of, and seek regulatory approvals for, its product candidates, and begin to commercialize any approved products. If the clinical trials for any of the Company s products fail or produce unsuccessful results and those product candidates do not gain regulatory approval, or if any of its product candidates, if approved, fails to achieve market acceptance, the Company may never become profitable. Even if the Company achieves profitability in the future, it may not be able to sustain profitability in subsequent periods. The Company

intends to cover its future operating expenses through cash on hand and through additional financing from existing and prospective investors. The Company cannot be sure that additional financing will be available when needed or that, if available, financing will be obtained on terms favorable to the Company or to its stockholders.

As of December 31, 2016, the Company had cash, cash equivalents and investment securities totaling $133.0 million. While the Company expects that its existing cash, cash equivalents and investment securities will enable it to fund its operations and capital expenditure requirements for at least the next twelve months, having insufficient funds may require the Company to delay, reduce, limit or terminate some or all of its development programs or future commercialization efforts or grant rights to develop and market product candidates that it would otherwise prefer to develop and market on its own. Failure to obtain adequate financing could eventually adversely affect the Company s ability to operate as a going concern. If the Company raises additional funds from the issuance of equity securities, substantial dilution to its existing stockholders would likely result. If the Company raises additional funds by incurring debt financing, the terms of the debt may involve significant cash payment obligations as well as covenants and specific financial ratios that may restrict its ability to operate its business.

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2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Use of Estimates

The preparation of financial statements in conformity with United States generally accepted accounting principles (GAAP), requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities and expenses, and related disclosures. Significant estimates used in preparing the financial statements include those assumed in estimating expenses for the Company s pre-clinical studies and clinical trials, computing the valuation allowance on deferred tax assets, calculating stock-based compensation expense and for determining the value of leased property during the construction period for which the Company has been deemed the accounting owner. Actual results could differ from those estimates or assumptions.

Reclassifications

Certain reclassifications have been made to prior year amounts to conform to the current year presentation. These changes had no impact on the Company s total assets or reported net loss.

Cash, Cash Equivalents and Investment Securities

The Company considers all highly liquid investments with an original maturity of 90 days or less when purchased to be cash equivalents. Cash and cash equivalents represent bank demand deposits and amounts invested in money market funds.

Investment securities are considered to be available-for-sale and consist of government and government agency obligations, corporate notes and bonds and commercial paper. Investment securities are recorded at estimated fair value, and unrealized gains and losses for these securities are included in accumulated other comprehensive income or loss, a component of stockholders equity. The Company evaluates its investment securities as of each balance sheet date to assess whether those with unrealized loss positions are other-than-temporarily impaired. Impairments are considered to be other-than-temporary if they are related to deterioration in credit risk or if it is likely that the Company will sell the securities before the recovery of its cost basis. Realized gains and losses and declines in value judged to be other-than-temporary are determined based on the specific identification method. No other-than-temporary impairment charges have been recognized for any of the fiscal periods reported in these financial statements.

Fair Value of Financial Instruments

Financial assets and liabilities are measured at fair value, which 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 must maximize the use of observable inputs and minimize the use of unobservable inputs. The valuation of assets and liabilities is subject to fair value measurements using a three tiered approach, and fair value measurement is classified and disclosed in one of the following categories:

Level 1: Quoted prices in active markets for identical 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 that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities; or

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.

Cash, cash equivalents, investment securities are carried at fair value (see Note 3). Other current assets, accounts payable and accrued expenses, and other liabilities are carried at costs which represents a reasonable estimate of fair value due to the short-term nature of these items. The carrying value of the term debt approximates its fair value as the interest rate and other terms are that which is currently available to the Company. Fair value estimates of these instruments at a specific point in time are made based on relevant market information. These estimates can be subjective, involve uncertainties and matters of judgment, and therefore cannot be determined with precision.

Credit Risk

Financial instruments that may subject the Company to credit risk consist of cash, cash equivalents, investment securities and term loan obligations. The Company maintains demand deposits with financial institutions in amounts that typically exceed the amount of federal insurance provided on such deposits. Investment securities are invested in accordance with the Company s investment policy which specifies the categories, allocations, and ratings of securities that may be considered for investment. Management does not believe that the Company s cash equivalents and investment securities have a significant risk of default or illiquidity. The primary exposure to market risk with respect to investment securities and the Company s term loans is the risk that prevailing interest rates change causing the value of the investment securities and the value of the obligation owed under term loans to fluctuate.

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Sources of supply

The Company relies on third-party manufacturers and single source third-party suppliers to manufacture its preclinical and clinical drug supplies for use in the conduct of preclinical studies and clinical trials. If the Company s third-party manufacturers are unable to continue manufacturing our preclinical and clinical drug supplies, or if it lost the single source suppliers used in the manufacturing process, it may not be able to meet the demand to support ongoing clinical trials. The Company also does not currently have arrangements in place for the commercial supply of bulk drug substance or drug products. It may not be able to establish these or any other supply relationship when needed, on reasonable terms, or at all. Any failure to secure sufficient supply of its product candidates for preclinical or clinical testing or, in the future, for commercial purposes, would materially harm the Company s operations and financial results.

Property and Equipment

Property and equipment are recorded at cost and depreciated using the straight-line method over the estimated useful lives of the related assets. Asset lives range from three to seven years, or, in the case of leasehold improvements, over the lesser of the useful life of the related asset or the lease term. Maintenance and repairs are expensed as incurred.

The Company establishes assets and corresponding financing liabilities for the construction costs incurred under build-to-suit lease arrangements when it is determined that the Company has taken construction risks during the construction period and is deemed the accounting owner of the property during construction. At the end of the construction period, the Company assesses whether the arrangement qualifies for sales recognition under the sale-leaseback accounting guidance in ASC 840.

The Company reviews property and equipment for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. An impairment loss would be recognized when estimated future undiscounted cash flows relating to the asset are less than its carrying amount. An impairment loss is measured as the amount by which the carrying amount of an asset exceeds its fair value. To date, the Company has not experienced any significant impairment losses on its property and equipment.

Research and Development

Costs incurred in connection with research and development activities are expensed as incurred. Research and development expenses consist of (i) external research and development expenses incurred under arrangements with third parties, such as contract research organizations, investigational sites and consultants; (ii) employee-related expenses, including salaries, benefits, travel and stock compensation expense; (iii) the cost of acquiring, developing and manufacturing clinical study materials; (iv) facilities and other expenses, which include direct and allocated expenses for rent and maintenance of facilities and laboratory and other supplies, and (v) license fees and other expenses relating to the acquisition of rights to development programs.

The Company enters into consulting, research and other agreements with commercial firms, researchers, universities and others for the provision of goods and services. Under such agreements, the Company may pay for services on a monthly, quarterly, project or other basis. Such arrangements are generally cancellable upon reasonable notice and payment of costs incurred. Costs are considered incurred based on an evaluation of the progress to completion of specific tasks under each contract using information and data provided to the Company by its clinical sites and vendors and other information. These costs consist of direct and indirect costs associated with specific projects, as well as fees paid to various entities that perform certain research on behalf of the Company.

In certain circumstances, the Company is required to make advance payments to vendors for goods or services that will be received in the future for use in research and development activities. In such circumstances, the advance payments are deferred and are expensed when the activity has been performed or when the goods have been received.

The Company expenses all costs as incurred in connection with patent applications (including direct application fees, and the legal and consulting expenses related to making such applications) and such costs are included in general and administrative expenses.

Clinical Trial and Pre-Clinical Study Accruals

The Company makes estimates of accrued expenses as of each balance sheet date in its financial statements based on the facts and circumstances known to it at that time. Accrued expenses for pre-clinical studies and clinical trials are based on estimates of costs incurred and fees that may be associated with services provided by contract research organizations, clinical trial investigational sites, and other related vendors. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and the completion of milestones. In accruing service fees, management estimates the time period over which services will be performed and the level of effort to be expended in each period. If possible, the Company obtains information regarding unbilled services directly from these service providers. However, the Company may be required to estimate these services based on other information available to it. If the Company underestimates or overestimates the activity or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods.

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Income Taxes

Deferred income taxes are recognized for the tax consequences in future years of differences between the tax basis of assets and liabilities and their financial reporting amounts at each year end based on enacted tax laws and statutory tax rates applicable to the periods in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized. Income tax expense is the combination of the tax payable for the year and the change during the year in deferred tax assets and liabilities. The Company follows the accounting guidance on accounting for uncertainty in income taxes. The guidance prescribes a recognition threshold and measurement attribute criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more likely than not to be sustained upon examination by taxing authorities based on the technical merits of the position.

Stock-Based Compensation

Stock-based compensation cost for equity awards to employees and directors is measured at the grant date based on the estimated fair value of the award using the Black-Scholes option-pricing model. The value of the award that is ultimately expected to vest is recognized as an expense under the straight-line method over the requisite service period (generally the vesting period of the equity grant). Any changes to the estimated forfeiture rates are accounted for prospectively.

Stock options issued to non-employees are accounted for at their estimated fair values determined using the Black-Scholes option-pricing model. The fair value of options granted to non-employees is re-measured as they vest, and the resulting increase in value, if any, is recognized as an expense during the period the related services are rendered.

Comprehensive Income (Loss)

Comprehensive income or loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources. The Company s only component of other comprehensive income or loss is unrealized gains or losses on its available-for-sale investment securities. Comprehensive gains (losses) have been reflected in the statements of operations and comprehensive loss and as a separate component in the statements of stockholders equity for all periods presented.

Net Loss per Share

Basic and diluted net loss per share has been computed by dividing net loss by the weighted average number of common shares outstanding. The calculations of net loss per share exclude potentially dilutive securities (consisting of outstanding options, warrants and restricted stock units) of approximately 5.5 million and 5.4 million shares as of December 31, 2016 and 2015, respectively, as inclusion of these securities would be anti-dilutive for each of the years shown in the financial statements given the net loss position of the Company.

Recently Adopted Accounting Standards

In April 2015, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2015-03 which requires presentation of debt issuance costs as a direct deduction from the carrying amount of a recognized debt liability on the balance sheet rather than as an asset. The Company adopted this guidance at the beginning of fiscal 2016. This accounting treatment was applied retroactively to amounts presented in the Company s

balance sheet as of December 31, 2015. This change had no impact on the Company s previously reported results of operations.

In August 2014, the FASB issued ASU 2014-15, *Disclosure of Uncertainties about an Entity s Ability to Continue as a Going Concern*. The amendment requires management to evaluate, for each annual and interim reporting period, whether there are conditions and events, considered in the aggregate, that raise substantial doubt about an entity s ability to continue as a going concern within one year after the date the financial statements are issued or are available to be issued. If substantial doubt is raised, additional disclosures around management s plan to alleviate these doubts are required. This update became effective for fiscal years ending after December 15, 2016, and as such, the Company adopted this standard for its year ended December 31, 2016. Adoption of this standard did not have a significant impact on the Company s financial statements or the related disclosures therein.

In November 2015, the FASB issued ASU No. 2015-17, *Income Taxes (Topic 740) Balance Sheet Classification of Deferred Taxes*. The amendments in this update simplify the presentation of deferred income taxes by requiring that deferred tax liabilities and assets be classified as noncurrent in a classified statement of financial position. This ASU is effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. The Company early adopted this guidance on a prospective basis for its year ended December 31, 2016. The adoption of this guidance did not have a significant impact on the Company s financial statements.

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Recent Accounting Pronouncements

On August 26, 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows* (Topic 230). This update affects all entities that are required to present a statement of cash flows and provide guidance and clarity on certain cash flow classification aspects. This update addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice. The ASU is effective for public companies for fiscal years beginning after December 15, 2017 and interim periods within those fiscal years, and early adoption is permitted. The Company is currently evaluating the impact, if any, of adopting this guidance on our financial statements.

In March 2016, the FASB issued ASU 2016-09, *Compensation Stock Compensation: Improvements to Employee Share-Based Payment Accounting*, which amended previous guidance on employee share-based payment accounting. This update involves several aspects of the accounting for share-based payment transactions, including income tax effects, forfeitures and classifications on the statement of cash flows. This guidance is effective for the Company s fiscal year beginning January 1, 2017. The Company does not believe that adoption of this guidance will have a material impact on its financial position or results of operations.

In February 2016, the FASB issued ASU 2016-02, *Leases*, which is intended to increase the transparency and comparability among organizations by recognizing lease assets and lease liabilities on the balance sheet and disclosing key information about leasing arrangements. In order to meet that objective, the new standard requires recognition of the assets and liabilities that arise from leases. A lessee will be required to recognize on the balance sheet the assets and liabilities for leases with lease terms of more than 12 months. The new standard is effective for public companies for the Company s fiscal year beginning January 1, 2019, and early adoption is permitted. The Company is currently evaluating the potential impact of this guidance on its financial statements and related financial statement disclosures.

In January 2016, the FASB issued ASU 2016-01, *Financial Instruments: Recognition and Measurement of Financial Assets and Financial Liabilities*. This update addresses certain aspects of the recognition, measurement, presentation, and disclosure of financial instruments. The new standard is effective for the Company s fiscal year beginning January 1, 2018. The Company is currently evaluating the potential impact of this guidance on its financial statements and related financial statement disclosures.

3. INVESTMENT SECURITIES

The Company reports its available-for-sale investment securities at their estimated fair values based on quoted market prices for identical or similar instruments. Following is a summary of the available-for-sale investments held by the Company as of the dates below (*in thousands*):

	As of December 31, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
Available-for-sale investment securities:				
Commercial paper	$ 8,996	$	$	$ 8,996
Corporate debt securities	49,179	1	(55)	49,125
U.S. government and agency obligations	50,568	1	(70)	50,499
Total	$ 108,743	$ 2	$ (125)	$ 108,620

	As of December 31, 2015			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
Available-for-sale investment securities:				
Commercial paper	$ 7,992	$	$	$ 7,992
Corporate debt securities	94,959	3	(180)	94,782
U.S. government and agency obligations	23,064		(72)	22,992
Total	$ 126,015	$ 3	$ (252)	$ 125,766

All of the Company s available-for-sale investment securities held at December 31, 2016, had maturity dates of less than 24 months. The Company determines the appropriate designation of investments at the time of purchase and reevaluates such designation as of each balance sheet date. Securities classified as short-term investments have maturity dates of less than one year from the balance sheet date, while those classified as long-term have maturity dates of greater than one year from the balance sheet date. The cost of securities sold is based on the specific identification method. The Company has not realized any significant gains or losses on sales of

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available-for-sale investment securities during any of the periods presented. Amortization of premiums, accretion of discounts, interest, dividend income, and realized gains and losses are included in investment income.

None of the Company s available-for-sale investment securities were in a material unrealized loss position at December 31, 2016. The Company reviewed its investment holdings as of December 31, 2016, and determined that its unrealized losses were not considered to be other-than-temporary based upon (i) the financial strength of the issuing institution and (ii) the fact that no securities have been in an unrealized loss position for twelve months or more. As such, the Company has not recognized any impairment in its financial statements related to its available-for-sale investment securities.

4. FAIR VALUE MEASUREMENTS

Available-for-sale investment securities consist of highly liquid, investment grade debt securities. The Company determines the fair value of these securities based upon one or more valuations reported by its investment accounting and reporting service provider. This service provider values securities using a hierarchical security pricing model that relies primarily on valuations provided by an industry-recognized valuation service. Such valuations may be based on trade prices in active markets for identical assets or liabilities (Level 1 inputs) or valuation models using inputs that are observable either directly or indirectly (Level 2 inputs), such as quoted prices for similar assets or liabilities, yield curves, volatility factors, credit spreads, default rates, loss severity, current market and contractual prices for the underlying instruments or debt, and broker and dealer quotes, as well as other relevant economic measures.

The fair value of cash, cash equivalents and available-for-sale investment securities were as follows (*in thousands*):

	As of December 31, 2016				As of December 31, 2015			
	Level 1	**Level 2**	**Level 3**	**Total**	**Level 1**	**Level 2**	**Level 3**	**Total**
Cash and cash equivalents	$ 24,340	$	$	$ 24,340	$ 46,383	$	$	$ 46,383
Investment securities:								
Commercial paper		8,996		8,996		7,992		7,992
Corporate debt securities		49,125		49,125		94,782		94,782
U.S. government and government agency obligations	50,499			50,499	22,992			22,992
Total investment securities	50,499	58,121		108,620	22,992	102,774		125,766
Total assets measured at fair value	$ 74,839	$ 58,121	$	$ 132,960	$ 69,375	$ 102,774	$	$ 172,149

The Company s policy is to recognize transfers between levels of the fair value hierarchy on the date of the event or change in circumstances that caused the transfer. There were no transfers into or out of Level 1, 2, or 3 for the years ended December 31, 2016 and 2015.

Instruments Not Recorded at Fair Value on a Recurring Basis

The estimated fair value of the term loan is determined by Level 2 inputs and is based primarily on quoted market prices for the same or similar issues. The recorded value of the Company s term loan approximates the current fair value due to the proximity to when the term loan was negotiated.

5. BALANCE SHEET DETAILS

Property and Equipment

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

	December 31, 2016	December 31, 2015
Lab and manufacturing equipment	$ 7,656	$ 6,941
Computer and office equipment	1,762	1,145
Leasehold improvements	374	2,349
Property and equipment at cost	9,792	10,435
Less accumulated depreciation and amortization	(3,522)	(2,671)
Subtotal	6,270	7,764
Construction in process (see below)		11,000
Property and equipment, net	$ 6,270	$ 18,764

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Lab and manufacturing equipment includes assets acquired in 2014 under leases accounted for as capital leases. These assets had an original acquisition value of $0.6 million, and a net book value of $0.4 million and $0.5 million as of December 31, 2016 and 2015, respectively. Depreciation related to these assets totaled $0.1 million in both fiscal 2016 and 2015, and $17,000 in fiscal 2014.

Other Long-Term Liabilities

Other long-term liabilities consisted of the following (*in thousands*):

	December 31, 2016	December 31, 2015
Leased facility financing obligation (see below)	$	$ 11,000
Final loan fee obligation to lender (see note 6)	1,600	930
Other long-term liabilities	1,510	234
Total	$ 3,110	$ 12,164

Construction in Process and Leased Facility Financing Obligation

In October 2015, the Company entered into an agreement for the lease of laboratory and office space on a build-to-suit basis for its new headquarters location in San Diego, California. The buildings that house the leased space as well as the space leased by the Company underwent a significant renovation, which was completed in October 2016. Based on the terms of the lease agreement and authoritative literature, the Company was determined to bear substantially all of the construction-related risks during the construction period and was deemed the owner of the building for accounting purposes during the construction period. As a result, the Company s balance sheet at December 31, 2015, included a fixed asset (construction in process) and a corresponding leased facility financing obligation of $11.0 million, respectively, reflecting the estimated replacement cost of these buildings at lease inception and the accumulated build-out costs incurred subsequent to lease inception. At the time the Company took possession of the properties in the fourth quarter of 2016, it determined that it had transferred the risks of ownership back to the owner of the properties. As such, the Company satisfied the requirements for sale-leaseback accounting treatment and it derecognized both the building assets and the related liability in the fourth quarter of 2016.

6. NOTE PAYABLE

In June 2016, the Company entered into a term loan facility with Silicon Valley Bank, as collateral agent (SVB), and Oxford Finance LLC (Oxford and collectively with SVB, the Lenders). Under the loan facility, the Company received initial funding of $32.0 million, substantially all of which was used to repay the Company s prior loan with SVB. The Company considered authoritative literature which states that modifications or exchanges are considered extinguishments with gains or losses recognized in current earnings if the terms of the new debt and original instrument are substantially different. The Company determined that for SVB s portion of the new facility, the terms are not substantially different from the prior loan and should be accounted for as a debt modification with previously deferred financing costs amortized as an adjustment of interest expense over the remaining term of the modified debt using the interest method. The Company determined that the portion of the old facility with SVB that was not assumed by SVB under the new facility should be accounted for as a debt extinguishment with fees paid to the lender and previously deferred financing costs included in the calculation of loss on debt extinguishment. The Company recorded a loss on debt extinguishment of $0.7 million during the second quarter of fiscal 2016. Borrowings under the

new facility will bear interest at a rate equal to the Prime Rate plus 4.35% (8.10% at December 31, 2016) and have interest only payments for twenty-four months, followed by a principal amortization period of thirty-six months. The interest only period will be extended, however, by an additional six months in the event of either (i) the Company raising sufficient capital or (ii) the Company receiving certain clinical trial data. In the event that the interest only period is extended, the principal amortization period will be reduced to thirty months.

Upon the maturity date, the Company must make a final lump-sum payment of 5.0% of the full amount of the loan funded ($1.6 million). The fair value of the final payment has been recorded as a debt discount which is being amortized to interest expense over the term of the loan agreement. The Company may elect to prepay all amounts owed prior to the maturity date provided that a prepayment fee is also paid, equal to 2% of the amount prepaid if the prepayment occurs on or prior to June 30, 2017, or 1% of the amount prepaid if the prepayment occurs thereafter. Under the facility, the Company also has a conditional option to receive an additional $10.0 million loan tranche (the Second Tranche). The Second Tranche may be drawn down by the Company at any time from April 7, 2017, to August 31, 2017, provided that the Company has received certain clinical trial data and subject to other customary conditions for funding.

In connection with this facility, the Company issued warrants to the Lenders to purchase an aggregate of approximately 94,116 shares of its common stock. The warrants are exercisable immediately, have a per-share exercise price of $5.10 and have a term of seven years. If the Company draws down the Second Tranche, at that time it will issue to the Lenders additional warrants which will be

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exercisable immediately and have a term of seven years. Those warrants will be exercisable for an aggregate number of shares equal to $150,000 (which is 1.5% of the principal amount of the Second Tranche) divided by the lower of (a) the trailing 10-day average of the closing price of the Company s common stock on the NASDAQ Capital Market prior to the funding date of the Second Tranche and (b) the closing price of the Company s common stock on the NASDAQ Capital Market on the funding date of the Second Tranche, at an exercise price equal to such divisor. The warrants qualify for equity classification and the fair value of the warrants has been recorded as a debt discount which is being amortized to interest expense over the term of the loan agreement.

Future minimum principal payments under the Company s note payable are as follows (*in thousands*):

Year ending December 31,	*Minimum Payments*
2017	$
2018	5,333
2019	10,667
2020	10,667
2021	5,333
Total	$ 32,000

The Company is bound by certain affirmative and negative covenants setting forth actions that it must and must not take during the term of the loan agreement, including a prohibition on the payment of dividends. Under the loan agreement, the Company must also maintain the majority of its cash in accounts at SVB. Upon the occurrence of an event of default, subject to cure periods for certain events of default, all amounts owed by the Company thereunder shall begin to bear interest at a rate that is 3% higher than the rate that is otherwise applicable and may be declared immediately due and payable by the Lenders. The Company has granted SVB, as collateral agent for the ratable benefit of the Lenders, a security interest in substantially all of its personal property, rights and assets, other than intellectual property, to secure the payment of all amounts owed under this agreement. The Company has also agreed not to encumber any of its intellectual property without the required lenders prior written consent.

The Loan Agreement also contains customary indemnification obligations and customary events of default, including, among other things, our failure to fulfill certain obligations of the Company under the Loan Agreement and the occurrence of a material adverse change which is defined as a material adverse change in the Company s business, operations, or condition (financial or otherwise), a material impairment of the prospect of repayment of any portion of the loan, or a material impairment in the perfection or priority of lender s lien in the collateral or in the value of such collateral. In the event of default by the Company under the Loan Agreement, the lender would be entitled to exercise its remedies thereunder, including the right to accelerate the debt, upon which the Company may be required to repay all amounts then outstanding under the Loan Agreement, which could harm the Company s financial condition. As of December 31, 2016, the Company was in compliance with all covenants under the Loan Agreement and there had been no material adverse change.

7. ASSET ACQUISITION

In March 2015, under the terms of an asset purchase agreement with Cephalon, Inc. (Cephalon), an indirect wholly owned subsidiary of Teva Pharmaceutical Industries Ltd. (Teva), the Company acquired certain assets relating to

certain oncology development programs, including Cephalon s right, title and interest in and to certain intellectual property, compounds, products, contracts, records, data and development supplies related to the Company s RXDX-105 and RXDX-106 programs (the Purchased Assets), and assumed certain related commitments. As consideration for the Purchased Assets, the Company issued to Cephalon 1,500,000 shares of common stock and assumed certain other third-party obligations. The Company did not acquire any marketable products, established customer or employee bases, or any established business, management, operational or resource management processes. Accordingly, the Company recorded this transaction as an asset purchase as opposed to a business combination. The acquired assets were in various stages of drug development, ranging from preclinical stage to Phase 1 clinical trials, and the development plans were still being formulated and were not complete as of the date of acquisition. As the success of the Company s commercialization of these acquired compounds was uncertain and the assets in question had no alternative future uses, the Company recorded an in-process research and development charge of approximately $11.9 million during the first quarter of 2015 related to this transaction based on the value of the net assets exchanged for the Teva assets. Under the provisions of the asset purchase agreement, the Company also paid approximately $0.9 million to Cephalon for drug development supplies, which was included in research and development expenses during the first quarter of 2015.

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8. LICENSE AGREEMENTS

Entrectinib

The Company entered into a license agreement with Nerviano Medical Sciences S.r.l. (NMS) on October 10, 2013, which was amended on October 25, 2013, became effective on November 6, 2013, and was later amended on December 12, 2014. The license grants the Company exclusive global rights to develop and commercialize entrectinib. The Company s development rights under the license are exclusive for the term of the agreement with respect to entrectinib and also, as to NMS, are exclusive for a five-year period with respect to any product candidate with activity against the target proteins of entrectinib, and include the right to grant sublicenses.

The Company is obligated under the license agreement to use commercially reasonable efforts to develop and commercialize a product based on entrectinib at its expense. When and if commercial sales of a product begin, the Company will be obligated to pay NMS tiered royalties ranging from a mid-single digit percentage to a low double digit percentage (between 10% and 15%) of net sales, depending on the amount of net sales, with standard provisions for royalty offsets to the extent it obtains any rights from third parties to commercialize the product. The license agreement also requires that the Company make development and regulatory milestone payments to NMS of up to $105.0 million in the aggregate if specified clinical study initiations and regulatory approvals are achieved across multiple products or indications. Life-to-date payments to NMS in connection with this agreement totaled $17.0 million as of December 31, 2016, and included an up-front payment of $7.0 million (paid in November 2013) and an initial milestone payment of $10.0 million (paid in December 2014). All payments under this agreement have been expensed as research and development (as no future benefit was determined to exist at the time of payment).

Taladegib

On November 6, 2015, the Company entered into a license, development and commercialization agreement with Eli Lilly and Company (Lilly) under which the Company received exclusive, global rights to develop and commercialize pharmaceutical products under the licensed technology (Licensed Products), including Lilly s product candidate taladegib. Taladegib is an orally bioavailable, small molecule hedgehog/smoothened antagonist that has achieved clinical proof-of-concept and a recommended Phase 2 dose in a Phase 1 dose escalation trial. The Company granted back to Lilly an exclusive license to develop and commercialize pharmaceutical products comprising taladegib in combination with certain other molecules (Combination Products). The Company also licensed the exclusive worldwide rights to the topical formulation of taladegib, which is a late preclinical development program for the potential treatment of patients with superficial and nodular basal cell carcinoma. In February 2016, the Company ceased all development activities relating to the topical taladegib program. Both parties rights under the agreement include the right to grant sublicenses. The Company is obligated under the agreement to use commercially reasonable efforts to develop and commercialize Licensed Products, at its expense. Both parties have a right to terminate the agreement if the other party enters bankruptcy, upon an uncured breach by the other party or if the other party challenges its patents relating to the licensed technology. The Company has been in discussions with Lilly regarding the optimal path forward for taladegib in the context of its pipeline priorities. In connection with these discussions Lilly has indicated that it believes that the Company may not have satisfied certain of its obligations to Lilly under the license agreement, but Lilly has also indicated an interest in achieving an amicable resolution with respect to this issue and the parties are continuing discussions consistent with this desire.

The terms of the license agreement provided for an up-front payment to Lilly of $2.0 million, plus the issuance to Lilly in a private placement of 1,213,000 shares of the Company s common stock. The Company included the up-front payment in research and development costs and recorded a charge of approximately $13.4 million during the fourth quarter of 2015 based on the value of the shares issued as equity in the fourth quarter of 2015. The license agreement

also requires that the Company makes development and sales milestone payments to Lilly of up to $38.0 million. In addition, a portion of the $30.0 million in gross proceeds provided to the Company by Lilly in a concurrent private placement of the Company s common stock to Lilly (in November 2015) has been earmarked for development of the product and payment of milestone obligations under the license agreement. When and if commercial sales of Licensed Products begin, the Company will be obligated to pay Lilly a mid-single digit royalty of net sales of Licensed Products. When and if commercial sales of Combination Products begin, Lilly will be obligated to pay the Company a mid-single digit royalty of net sales of Combination Products. Both parties royalty obligations are subject to standard provisions for royalty offsets to the extent a party is required to obtain any rights from third parties to commercialize the applicable products, or in the event of loss of exclusivity or generic competition.

RXDX-105 and RXDX-106

In connection with the March 2015 asset acquisition from Cephalon, the Company assumed all rights and obligations under the collaboration agreement dated November 3, 2006, as amended April 17, 2009, between Cephalon, Inc. and Daiichi Sankyo Company, Limited (Daiichi Sankyo), as successor-in-interest to Ambit Biosciences Corporation. The collaboration portion of the agreement ended in November 2009, but the agreement remains in effect on a product-by-product, country-by-country basis until all royalty obligations expire. Both parties have a right to terminate the agreement if the other party enters bankruptcy or upon an uncured breach by the other party. The Company may also terminate the agreement in its discretion upon 90 days written notice to Daiichi Sankyo.

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The Company is solely responsible for worldwide clinical development and commercialization of collaboration compounds, subject to the option of Daiichi Sankyo, exercisable during certain periods following completion of the first proof-of-concept study in humans and only with the consent of the Company, to co-develop and co-promote RXDX-105. If the Company decides to discontinue development of the RXDX-105 program, it must give written notice to Daiichi Sankyo, which will have the right to assume control of that program, subject to diligence obligations and payment of the milestones and royalties to the Company that would otherwise have been paid to Daiichi Sankyo had the Company maintained responsibility for the program.

The agreement requires the Company to make development, regulatory and sales milestone payments to Daiichi Sankyo of up to $44.5 million in the aggregate for RXDX-105, and up to $47.5 million in payments upon the achievement of development, regulatory and sales milestones for RXDX-106. When and if commercial sales of a product based on either of RXDX-105 or RXDX-106 begin, the Company will be obligated to pay Daiichi Sankyo tiered royalties ranging from a mid-single digit percentage to a low double digit percentage of net sales, depending on annual amounts of net sales, with standard provisions for royalty offsets to the extent it is required to obtain any rights from third parties to commercialize either RXDX-105 or RXDX-106. Royalties are payable to Daiichi Sankyo on a product-by-product, country-by-country basis beginning on the date of the first commercial sale in a country and ending on the later of 10 years after the date of such sale in that country or the expiration date of the last to expire licensed patent covering the product in that country.

9. COMMITMENTS AND CONTINGENCIES

Leases

In October 2015, the Company entered into a non-cancellable lease of laboratory and office space on a build-to-suit basis for its new headquarters location in San Diego, California. The buildings that house the leased space, as well as the space leased by the Company, underwent a significant renovation, which was completed in October 2016. The scope of the tenant improvements did not qualify as normal tenant improvements under the lease accounting guidance. Based on the authoritative literature, the Company was determined to bear substantially all of the construction-related risks during the construction period and was deemed the owner of the building for accounting purposes during the construction period. The renovation of the leased facility was completed in October 2016. At the time the Company took possession of the properties, it determined that it had transferred the risks of ownership back to the owner of the properties. As such, the Company satisfied the requirements for sale-leaseback accounting treatment and it derecognized both the building assets and the related liability in the fourth quarter of 2016.

The Company s obligation to pay rent commenced in October 2016. The lease includes a free rent period and escalating rent payments and has a ten-year term. The lease also contains a one-time provision to terminate the lease for all or a portion of the facilities, effective as of the end of the 72nd month after the lease commencement date, subject to the payment of a termination fee defined in the lease agreement. This lease is being accounted for as an operating lease.

The Company also leases other office space under operating leases that expire through 2018. These facility leases contain periodic rent increases that result in the Company recording deferred rent over the term of these leases.

Rental expense under operating leases was $1.5 million, $0.6 million and $0.5 million for 2016, 2015 and 2014, respectively. Included in 2016 operating results is ground rental expense of $0.5 million recorded during the construction period of the Company s new headquarters location.

The Company s non-cancellable future minimum annual lease payments under its operating leases for the years ending after December 31, 2016 are as follows *(in thousands):*

	Minimum Payments
2017	$ 2,552
2018	4,572
2019	4,593
2020	4,731
2021	4,873
Thereafter	4,162
Total minimum lease payments	$ 25,483

The Company has also entered into capital lease arrangements for the purchase of certain lab equipment. Future minimum lease payments under the Company s capital lease obligations totaled $0.2 million as of December 31, 2016.

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Clinical Trial Study Agreement Commitments

The Company has entered into agreements with several contract research organizations for clinical studies to be conducted both within and outside the U.S. for its product candidates. As of December 31, 2016, the total contracted cost under these arrangements was approximately $79.0 million, of which the Company had either paid or accrued total costs of approximately $30.6 million. These agreements run through various dates, with the longest term expected to run through 2020. These contracts can be terminated at any time with no more than 60 days notice, at which point the Company would be obligated to pay for costs incurred though the termination date.

Other matters

Although the Company is currently not a party to any material legal proceedings, in the normal course of business, the Company has been, and will likely continue to be, subject to claims, administrative proceedings or litigation incidental to its business that are either judged to be not material or that arise in the ordinary course of business from time to time, such as claims related to customer disputes, employment practices, wage and hour disputes, professional liability, licensure restrictions or denials, and patent infringement. Responding to such matters, regardless of whether they have merit, can be expensive and disruptive to normal business operations. Due to the uncertainties inherent in legal proceedings and litigation, the Company is not able to predict the timing or outcome of these matters. The Company could in the future incur judgments or enter into settlements of claims that could have an adverse effect on its results of operations in any particular period.

10. STOCKHOLDERS EQUITY

Authorized Shares

The Company is authorized to issue 150,000,000 shares of common stock and 10,000,000 shares of preferred stock, with the preferred stock having the rights, preferences and privileges that the Company s board of directors may determine from time to time. Each share of the Company s common stock is entitled to one vote, and all shares rank equally as to voting and other matters.

Stock Offerings

In May 2016, the Company completed a public offering of an aggregate of 9,200,000 shares of its common stock for net proceeds of approximately $53.9 million (net of transaction costs of approximately $3.6 million).

In November 2015, concurrent with its license agreement with Lilly (see Note 8), the Company issued and sold 1,500,000 shares of its common stock to Lilly for net proceeds of approximately $30.0 million (the transaction costs were negligible). The Company also entered into a registration rights agreement with Lilly pursuant to which the Company agreed to register the resale of the shares of the Company s common stock held by Lilly. The Company may be liable for liquidated damages if it fails to timely file, obtain effectiveness or maintain the effectiveness of the registration statement.

In June 2015, the Company completed a public stock offering providing for the issuance and sale to investors of an aggregate of 4,285,714 shares of its common stock for net proceeds of approximately $70.1 million (net of transaction costs of $4.9 million).

In March 2015, concurrent with its asset purchase agreement with Cephalon (see Note 7), the Company issued and sold 4,158,750 shares of common stock to Cephalon and several additional investors in a registered direct offering.

The net proceeds from this offering totaled approximately $41.4 million (net of transaction costs of $149,000).

In March 2014, the Company completed a public stock offering providing for the issuance and sale to investors of an aggregate of 6,031,750 shares of its common stock for net proceeds of approximately $51.6 million (net of transaction costs of $3.6 million).

At-The-Market Issuance Sales Agreement

In December 2015, the Company entered into an at-the-market issuance sales agreement (the Sales Agreement) with Cantor Fitzgerald & Co. (Cantor), pursuant to which the Company may issue and sell shares of its common stock from time to time, at the Company s option, through Cantor as its sales agent. The Company is not obligated to make any sales of its common stock under the Sales Agreement, and it may terminate its agreement with Cantor at any time. Any shares sold will be sold pursuant to an effective shelf registration statement on Form S-3. The Company will pay Cantor a commission of 3.0% of the gross proceeds of any such sales. The Company has reserved up to $33.0 million under its shelf registration statement for shares that may be issued under the Sales Agreement. Through December 31, 2016, the Company has not made any sales of shares in connection with this arrangement.

Common Stock Warrants

Warrants to purchase an aggregate of 153,472 shares of the Company s common stock were outstanding at December 31, 2016. These warrants have a weighted average exercise price of $5.75 per share and expire at various dates through June 2023.

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11. EQUITY AWARDS

Equity Incentive Plans

The Company may issue equity awards to either employees or non-employees under its Amended and Restated 2014 Incentive Award Plan (the 2014 Plan). The 2014 Plan provides for the issuance of up to 6,000,000 shares, plus one additional share for each option share granted under the Company s 2011 Incentive Award Plan (the 2011 Plan) that expires, is forfeited or is settled in cash subsequent to June 11, 2014. Options granted under the 2014 Plan may be subject to vesting and expire no more than ten years from their date of grant. The Company has equity awards outstanding that were granted under various predecessor equity award plans, however no additional equity grants may be made under these plans.

A summary of stock option activity during the year ended December 31, 2016, and other related information, is as follows:

	Options Outstanding	Weighted-Average Exercise Price	Weighted-Average Remaining Term	Aggregate Intrinsic Value
Balance at December 31, 2015	5,250,941	$ 9.16		
Granted	1,276,641	$ 8.17		
Exercised	(126,698)	$ 3.24		
Forfeited	(1,291,599)	$ 9.92		
Balance at December 31, 2016	5,109,285	$ 8.86	7.85	$ 834,601
Exercisable at December 31, 2016	2,284,866	$ 8.00	6.91	$ 760,794

As of December 31, 2016, an aggregate of 3,525,680 shares remain available for grant under the Company s equity incentive plan.

Fair Value of Equity Awards

The estimated weighted-average fair value of stock options granted during fiscal 2016, 2015 and 2014 was $5.25, $7.25 and $4.72 per share, respectively. The Company utilizes the Black-Scholes option pricing model to estimate the value of equity awards under its plans. The key valuation assumptions used in formulating these estimates include:

Volatility the measure of the amount by which a financial variable, such as a share price, has or is expected to fluctuate during a period. As the Company has not been publicly traded for a significant period, it uses the historical volatility of peer companies in order to estimate expected volatility.

Expected Life of the Option Term the period of time that the options granted are expected to remain unexercised. The expected life of the option term for employee option grants is estimated using the

simplified method. For non-employee awards, the Company uses the contractual term of the award.

Risk-Free Interest Rate the U.S. Treasury rate for the day of each option grant during the year having a term that most closely resembles the expected life of the option.

Dividend Yield the Company has never declared or paid dividends on common stock and has no plans to do so.

The weighted-average assumptions used to estimate the fair value of stock option grants were as follows:

	Year ended December 31,		
	2016	**2015**	**2014**
Volatility	77%	69%	65%
Expected life of option	6.4 years	6.2 years	6.0 years
Risk free interest rate	1.5%	1.7%	1.8%
Dividend yield	%	%	%

Forfeitures are estimated at the time of grant and revised in subsequent periods if actual forfeitures differ from those estimates.

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Restricted Stock Units (RSUs)

During fiscal 2016 and 2015, the Company issued 206,880 and 90,000 RSUs, respectively, to members of its management team. As of December 31, 2016, a total of 238,480 of these RSUs were outstanding and subject to future vesting through January 2021.

Stock-Based Compensation

The following table summarizes stock-based compensation expense for all equity awards, including RSUs, issued to employees and non-employees for the periods presented (*in thousands*):

	Year ended December 31,		
	2016	**2015**	**2014**
Included in research and development	$ 3,464	$ 2,576	$ 896
Included in general and administrative	4,257	2,769	1,387
Total	$ 7,721	$ 5,345	$ 2,283

Unrecognized stock-based compensation expense related to unvested awards granted under the Company s equity incentive plans totaled $15.5 million as of December 31, 2016, and is expected to be recognized over a weighted-average period of 2.6 years.

12. INCOME TAXES

The Company is subject to income taxes in the United States as well as certain state tax jurisdictions. The Company provides for income taxes under the liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between the financial reporting and tax bases of assets and liabilities, and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. Due to its operating losses, the Company has not recorded a current or deferred income tax expense or benefit since its inception. A reconciliation of the statutory federal income tax provision to the actual income tax provision is as follows (*in thousands*):

	Year ended December 31,		
	2016	**2015**	**2014**
Expected income tax benefit at federal statutory rate	$ (35,237)	$ (31,436)	$ (13,597)
State income tax benefit, net of federal benefit	(2,837)	(5,438)	(2,245)
Research credits	(3,480)	(1,854)	(1,118)
Intangible related to asset acquisition		(1,247)	
Uncertain tax positions	3,476	1,386	
Other	812	13	162
Change in valuation allowance	37,266	38,576	16,798
Income tax expense (benefit)	$	$	$

Included in the balance of unrecognized tax benefits at December 31, 2016 is $4.8 million that, if recognized, would not impact our income tax benefit or effective tax rate as long as our deferred tax asset remains subject to a full valuation allowance. We do not expect any significant increases or decreases to our unrecognized tax benefits within the next 12 months. The following table summarizes the changes in the amount of the Company s unrecognized tax benefits (*in thousands*):

	Year ended December 31,		
	2016	**2015**	**2014**
Beginning balance	$ 2,100	$	$
Increase (decrease) for prior year tax positions	5,267	2,100	
Increase (decrease) for current year tax positions			
Income tax expense (benefit)	$ 7,367	$ 2,100	$

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Accordingly, the Company s net deferred tax asset has been fully offset by a valuation allowance. The significant components of the Company s deferred tax assets are comprised of the following (*in thousands*):

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	December 31,	
	2016	2015
Net operating loss carryforwards	$ 68,427	$ 35,131
Tax credit carryforwards	6,571	3,224
Stock-based compensation	5,104	2,848
Accrued compensation	1,295	1,485
Intangible assets recognized for tax purposes	11,856	13,143
In process research and development charge	5,376	5,865
Other, net	680	846
Total deferred tax assets	99,309	62,542
Deferred tax liabilities (depreciation)	(610)	(1,060)
Valuation allowance	(98,699)	(61,482)
Net deferred tax assets	$	$

At December 31, 2016, the Company had unused federal and state net operating loss (NOL) carryforwards of $192.3 million and $138.8 million, respectively, which will begin to expire in 2031. Approximately $1.0 million of these carryforwards relate to excess tax deductions for stock compensation, the benefit of which will be recorded as additional paid-in capital if and when realized. At December 31, 2016, the Company also had federal and state research tax credit carryforwards of $4.4 million and $3.3 million, respectively. The federal carryforwards begin to expire in 2031, while the state carryforwards have no expiration.

The utilization of NOL and tax credit carryforwards to offset future taxable income may be subject to an annual limitation as a result of ownership changes that have occurred previously or may occur in the future. Under Sections 382 and 383 of the Internal Revenue Code (IRC), a corporation that undergoes an ownership change may be subject to limitations on its ability to utilize its pre-change NOLs and other tax attributes otherwise available to offset future taxable income and/or tax liability. An ownership change is defined as a cumulative change of 50% or more in the ownership positions of certain stockholders during a rolling three-year period. The Company has not completed a formal study to determine if any ownership changes within the meaning of IRC Section 382 and 383 have occurred. If an ownership change has occurred, the Company s ability to use its NOL or tax credit carryforwards may be restricted, which could require the Company to pay federal or state income taxes earlier than would be required if such limitations were not in effect.

The Company conducts intensive research and experimentation activities, generating research tax credits for Federal and state purposes under IRC section 41. The Company has not performed a formal study validating these credits claimed in the tax returns. Once a study is prepared, the amount of R&D tax credits available could vary from what was originally claimed on the tax returns.

While the Company is not currently under any tax related examination, the tax years from 2012 through 2016 remain subject to examination by the taxing jurisdictions to which the Company is subject. The Company may be assessed interest and penalties related to the settlement of tax positions, and such amounts would be recognized within income tax expense when assessed.

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13. QUARTERLY DATA (*unaudited*)

The following quarterly financial data, in the opinion of management, reflects all adjustments, consisting of normal recurring adjustments, necessary for a fair presentation of results for the periods presented *(in thousands, except per share amounts):*

	Year Ended December 31, 2016			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Research and development expenses	$ 19,781	$ 20,019	$ 16,626	$ 20,500
Total operating expenses	$ 25,008	$ 25,518	$ 22,771	$ 27,387
Net loss	$ (25,492)	$ (26,651)	$ (23,289)	$ (28,208)
Net loss per share basic and diluted	$ (0.79)	$ (0.70)	$ (0.56)	$ (0.68)

	Year Ended December 31, 2015			
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Research and development expenses (1)(2)	$ 20,215	$ 8,796	$ 10,432	$ 34,068
Total operating expenses	$ 22,982	$ 12,651	$ 14,289	$ 40,658
Net loss	$ (23,507)	$ (13,120)	$ (14,621)	$ (41,210)
Net loss per share basic and diluted	$ (1.15)	$ (0.51)	$ (0.49)	$ (1.32)

(1) First quarter 2015 results include an up-front payment of $0.9 million and a non-cash charge of approximately $11.9 million based on the value of 1,500,000 shares of common stock exchanged for the assets acquired from Teva (see Note 7).

(2) Fourth quarter 2015 results include an up-front payment of $2.0 million and a non-cash charge of approximately $13.4 million based on the value of 1,213,000 shares of common stock exchanged for the rights acquired from Lilly for the Company s taladegib product candidate (see Note 8).