Ignyta, Inc.
Form 10-K
February 28, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, DC 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2013

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: 333-183886

Ignyta, Inc.

(Exact Name of Registrant as Specified in its Charter)

Nevada	**59-3564984**
(State or Other Jurisdiction of	**(I.R.S. Employer**
Incorporation or Organization)	**Identification No.)**
11095 Flintkote Avenue, Suite D	
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:

None

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

None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes x 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 x 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). x 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. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. 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 x

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 x

As of June 28, 2013, the last business day of the registrant s most recently completed second quarter, there was no established public market for the registrant s common stock.

The number of outstanding shares of the registrant s common stock, par value 0.00001 per share, as of February 25, 2014 was 13,534,876.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive proxy statement to be filed with the Securities and Exchange Commission pursuant to Regulation 14A in connection with the registrant s 2014 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this Form 10-K. Such proxy statement will be filed with the Securities and Exchange Commission not later than 120 days following the end of the registrant s fiscal year ended December 31, 2013.

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IGNYTA, INC.

FORM 10-K ANNUAL REPORT

For the Fiscal Year Ended December 31, 2013

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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 discovery of potential product candidates and the preclinical and clinical testing of our product candidates;
- the early 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 other 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, 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 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

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, 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, 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 for Ignyta®, Methylome®, Trailblaze® and Actagene®, and have a pending trademark application for Oncolome . 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, our company, we, us, and our refer to Ignyta, Inc., a Nevada corporation, and its consolidated subsidiary, and the term Ignyta Operating refers to Ignyta Operating, Inc., a private Delaware corporation that, through a reverse merger acquisition completed on October 31, 2013, became our wholly owned subsidiary.

Ignyta and Ignyta Operating effected reverse stock splits of their capital stock at the ratios of 100-to-one and three-to-one, respectively, on October 31, 2013. Unless the context indicates or otherwise requires, all share numbers and share price data included in this Annual Report on Form 10-K have been adjusted to give effect to those reverse stock splits.

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Item 1. Business

Corporate Overview

General

Ignyta was incorporated under the laws of the State of Nevada on August 21, 2012, with the name Infinity Oil & Gas Company. Ignyta Operating was incorporated under the laws of the State of Delaware on August 29, 2011, with the name NexDx, Inc. Ignyta Operating changed its name to Ignyta, Inc. on October 8, 2012. On October 31, 2013, IGAS Acquisition Corp, a wholly owned subsidiary of Ignyta, merged with and into Ignyta Operating, and Ignyta Operating survived the merger and became our wholly owned subsidiary. Upon the closing of the merger, we ceased to be a shell company under applicable rules of the SEC. In connection with the closing of the merger, Ignyta changed its name to Ignyta, Inc. and Ignyta Operating changed its name to Ignyta Operating, Inc.

On October 31, 2013, Ignyta 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 Ignyta 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 Operating s preferred stock were voluntarily converted into shares of Ignyta Operating s common stock in accordance with Ignyta Operating s certificate of incorporation, and (ii) Ignyta Operating 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 Operating s capital stock gives retroactive effect to that reverse stock split.

Concurrent with the closing of the merger, Ignyta abandoned its pre-merger business plan in the oil and gas industry, and we now solely pursue the business of Ignyta Operating in the oncology drug development industry. The following discussion describes our current business.

On May 20, 2013, Ignyta Operating completed its acquisition of Actagene Oncology, Inc., or Actagene, which merged with and into Ignyta Operating on that date.

Emerging Growth Company and Smaller Reporting Company Status

The Jumpstart Our Business Startups Act of 2012, or 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. Additionally, Section 12b-2 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, establishes a class of company called a smaller reporting company, which generally is a company with a public float of less than $75 million as of the last business day of its most recently completed second fiscal quarter or, if such public float is $0, had annual revenues of less than $50 million during the most recently completed fiscal year for which audited financial statements are available. We currently qualify as both an emerging growth company and a smaller reporting company.

As an emerging growth company and a smaller reporting company, 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 those classifications, 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.

Neither an emerging growth company nor a smaller reporting company is 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.

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A company that is either an emerging growth company or a smaller reporting 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.

A company that is either an emerging growth company or a smaller reporting 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. Smaller reporting companies are also eligible to provide such reduced financial statement disclosure in annual reports on Form 10-K.

For as long as we continue to be an emerging growth company and/or a smaller reporting company, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of those respective classifications. 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. We will remain a smaller reporting company until we have a public float of $75 million or more as of the last business day of our most recently completed second fiscal quarter, and we could retain our smaller reporting company status indefinitely depending on the size of our public float.

Business Overview

We are a precision medicine biotechnology company dedicated to discovering or acquiring, then developing and commercializing, precisely targeted new drugs for cancer patients whose tumors harbor specific molecular alterations. We are pursuing an integrated drug and diagnostic, or Rx/Dx, strategy, where we anticipate pairing each of our product candidates with biomarker-based companion diagnostics, developed by us or by third parties with which we may partner, that are designed to identify the patients that are most likely to benefit from the use of the drugs we may develop. Our current development plans focus on two product candidates: RXDX-101, a tyrosine kinase inhibitor directed to the Trk family tyrosine kinase receptors (TrkA, TrkB and TrkC), ROS1 and ALK proteins, which is in a Phase I/II clinical study in molecularly defined patient populations for the treatment of solid tumors; and RXDX-102, a tyrosine kinase inhibitor directed to the Trk family tyrosine kinase receptors. As a result of the preliminary Phase I results relating to RXDX-101 that we have seen to date, we have decided to designate RXDX-102 as a back-up compound to RXDX-101. Accordingly, we will not devote further development resources to RXDX-102 unless the development program for RXDX-101 is unsuccessful.

Tyrosine kinases are enzymes that transfer phosphate groups from adenosine triphosphate (ATP) to cellular proteins and can function as an on/off switch for cellular functions, including cancer signaling. We acquired exclusive global development and marketing rights to RXDX-101 and RXDX-102 under a license agreement with NMS which became effective in November 2013. We are also pursuing three discovery stage programs, Spark-1, Spark-2 and Spark-3, directed to emerging oncology targets identified through mining our database of information from proprietary and publicly available tumor samples, called Oncolome .

We currently have no products that have obtained marketing approval in any jurisdiction. We have not generated revenues since inception and do not expect to do so in the foreseeable future due to the early stage nature of our

current product candidates. We had net losses for the year ended December 31, 2013 of $14.2 million, and we had an accumulated deficit as of December 31, 2013 of $15.6 million.

From our inception, we have focused on discovering novel biomarkers that define diseases based on our belief that such biomarkers could provide rich biological insight into the underlying pathophysiology that drives the clinical symptomatology of those diseases. Biomarkers are substances detectable in the human body that can indicate presence or risk of a certain disease or disease subtype. One of our core platforms for revealing multivariate biomarkers that characterize diseases of interest is epigenetic analysis, particularly assessment of DNA methylation signatures. Epigenetics is the study of heritable changes in gene activity that are not caused by changes in DNA sequence, and DNA methylation is a specific type of epigenetic phenomenon that involves the chemical addition of a methyl group to DNA, which addition can impact the activity of that gene. A methylation signature is a specific pattern of differential DNA methylation that can serve as a biomarker that is indicative of a certain disease or disease subtype. When individual DNA sites have a different presence or absence of methyl groups in one individual compared to another individual or group of individuals, we refer to this as differential methylation.

Our initial business strategy was to use epigenetic biomarkers to develop new biomarker-based molecular diagnostic assays to help physicians differentially diagnose clinically confounding diseases, particularly chronic autoimmune and rheumatic

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diseases. However, in part due to macroeconomic challenges facing the molecular diagnostics industry, we determined that a more valuable deployment of our biomarker discovery engine would be to seek biomarkers that can serve as novel disease targets for therapeutic intervention. As a consequence, in May 2013, we acquired Actagene, a discovery stage precision medicine company applying genomic insights to discover new biomarkers and targets for cancer therapeutics. With the acquisition of Actagene we added important members to our management and drug discovery team, which is utilizing genetic and epigenetic analysis to discover and understand genes that are inappropriately activated in tumors. Our current focus is to identify genes and pathways that are altered in tumors of interest and to then acquire or develop drugs that target the proteins encoded by those genes and test those drugs in precise patient populations who have the underlying molecular alteration that our product candidates seek to address.

To identify molecular alterations that drive cancers, we mine both publicly available, as well as proprietary, tumor repositories to seek genetic (e.g., sequence mutations, fusions, inversions, translocations, copy number variants) and epigenetic (e.g., differential DNA methylation) changes that are common across cancers. We aggregate these tumor data along with detailed de-identified (no name, address, date of birth, or person-specific information) patient phenotypic information, which generally consists of observable physical or biochemical characteristics, into our proprietary in-house Oncolome database. Our Oncolome database currently consists of data from hundreds of proprietary tumor samples, as well as publicly available data from tens of thousands of tumor samples.

We currently pursue a two-pronged strategy to leverage the biomarker insights that we have gained through our genetic and epigenetic mining of our Oncolome database, as well as the knowledge of cancer biology of our management and drug discovery team.

In the first case, when we identify a molecular alteration that is driving the growth of tumors in cancers of interest and if there is already a company(ies) developing a product candidate(s) that targets that specific molecular alteration, we plan to seek to in-license what we believe to be the most promising or most advanced product candidate(s) available for licensing. This approach is exemplified by our in-license of RXDX-101 and RXDX-102 from Nerviano Medical Sciences, S.r.l., or NMS, in November 2013. We believe that RXDX-101 is one of the most clinically advanced inhibitors of TrkA, TrkB and TrkC, three targets that we believe to be activating alterations in several cancers with a substantial unmet medical need. RXDX-101 also has been observed to have potent activity against ROS1, another cancer target against which there are no approved products, and ALK, a clinically and commercially validated oncology target. We believe that this agent has the potential to be a first-in-class drug against important molecular targets that are driving alterations in various cancers.

In the second case, when we identify an activating molecular alteration that drives the growth of tumors in cancers of interest and there is no known company(ies) developing a product candidate(s) that targets that specific molecular alteration, we plan to seek to initiate target validation and drug discovery activities against that molecular target. This approach is exemplified by our Spark programs. To date, we have identified six molecular targets, denoted Spark-1 through Spark-6, that appear to be commonly altered in different cancer tissues. To our knowledge, no other commercial entity is currently developing clinical-stage product candidates that are specifically directed to these molecular targets. We have prioritized three of these six targets, denoted Spark-1, Spark-2 and Spark-3, and have initiated target validation and drug discovery activities against some of these molecular targets.

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 drug discovery and management team. Key aspects of our core drug discovery capabilities include the ability to perform x-ray crystallography on protein targets, conduct *in silico* structure-based drug design and run virtual chemistry screens. Once compounds with activity against our target have been identified by those or other tests and procedures, our drug discovery and scientific team further pursues the drug development process. 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.

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 cause 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, estimated that, in 2013, there would be approximately 1.6 million new cases of cancer and approximately 580,000 deaths from cancer in the United States. The World Health Organization estimated that 7.6 million people worldwide died of cancer in 2008. According to ACS data, lung, colon and rectal, breast and prostate cancer are the most prevalent cancers in the United States.

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The most common methods of treating patients with cancer are surgery, radiation and drug therapy, or chemotherapy. 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 systemic chemotherapy when the cancer has spread beyond the primary site or cannot otherwise be treated through surgery. The goal of chemotherapy 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, chemotherapy entails the administration of several different drugs in combination. Over the past several decades, chemotherapy has been evolving from non-specific drugs that kill both healthy and cancerous cells, to drugs that target specific molecular pathways involved in cancer and, more recently, to therapeutics that target specific activating alterations that are the drivers of cancer.

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 because of either a specific genetic alteration primarily found in cancer cells but not in normal cells, or a target that cancer cells are more dependent on for their growth than normal cells. These drugs focus on eradicating processes that help the cancer cell survive, but not on the oncogenes, which are the drivers or cause of the cancer itself.

Oncogene-Targeted Therapies. A more recent approach to pharmacological cancer treatment is to develop drugs that affect the drivers that cause uncontrolled growth of cancer cells because of a specific activating molecular alteration. In some cases these agents may be initially identified as targeted therapeutics without knowledge, at the time of development, of the underlying genetic change causing the disease. One primary shortcoming of this approach is that historically it has not been pursued systematically, but rather has tended to follow a conventional trial and error approach to drug discovery. Clinical development of oncogene-targeted therapies has involved the treatment of large populations from which a defined subpopulation that responds to treatment is identified through post-hoc analysis, after the trial has been completed. As a result, this approach can be time-consuming and costly, with success often uncertain.

Strategy

Our goal is to become a leading precision medicine oncology company by developing the next generation of therapeutics that treat cancer by targeting specific oncogenic activating molecular alterations and the corresponding patient populations. We believe our competitive advantage lies at the nexus of our two fundamental approaches: (1) a bottom up, data driven, unbiased, genome-wide multi-omics (e.g., DNA sequence, DNA methylation, DNA expression and protein expression) approach to mining extensive tumor data to identify activating alterations and their key biomarkers; and (2) a top down drug hunter approach of applying our senior scientific leadership team s many decades of successful cancer drug discovery and development experience. Key elements of our strategy are to:

Utilize public and proprietary sources of tumor samples and cancer data so that we are informed by a rich knowledge base. We have assembled a proprietary database of hundreds of tumor samples from primary human tumors from multiple solid tissues and hematological cancers. We supplement our proprietary database of tumor data by electronically integrating publicly available databases of tumor data. The combined database, with data from tens of thousands of tumor samples, is called Oncolome™. Oncolome consists of elements such as DNA sequences, gene copy number variants, and RNA transcript levels. This database also contains information on patient characteristics (such as age, gender, diagnosis and treatments) and, in some cases, analysis from such patients of ex-vivo chemosensitivity of their tumor cells to approved anticancer agents. We apply disciplined bioinformatic mining strategies and complex biostatisical algorithms to the data available in our Oncolome database, with the goal of identifying non-obvious trends and biomarkers that indicate activating alterations that drive cancer biology.

Apply a multi-omics approach to discover activating molecular alterations that drive cancer biology. We believe that genetic insight can be very valuable in understanding cancer biology, but that the exploration of biological factors in addition to genetics can provide a more comprehensive understanding of the precise activating molecular

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alterations that drive oncogenicity. Thus, when we mine our Oncolome database to seek new cancer biomarkers and potential drug targets, we often explore epigenetic phenomena, such as DNA methylation patterns, in addition to DNA sequencing and transcript counting. Our team has identified potential cancer targets that are marked by epigenetic alterations that we may not have identified had we applied a genetic approach alone.

Leverage deep cancer biology expertise and systems biology understanding to identify the specific role of activating alterations. Our senior scientific leadership team has been involved with the discovery or development of multiple approved cancer drugs and has extensive experience with the pathways involved with tumor growth. We intend to apply this knowledge, along with gene pathway mapping software, to gain insight into the biomarkers that are revealed from our unbiased genome-wide mining of our Oncolome database. We believe that this approach could expose unique druggable targets that are actually distinct from the specific biomarkers or activating alterations that characterize the cancer of interest.

Deploy drug design tools to develop small molecule inhibitors of activating targets. Our team has extensive experience with x-ray crystallography, structure-based drug design and virtual screening, in addition to more traditional chemistry screening methods and medicinal chemistry. We believe that by using these tools, we can more efficiently discover novel chemical series that bind to and inhibit our protein targets without incurring the expense of developing and maintaining a large chemical library and automated high throughput screening infrastructure.

Employ a capital-efficient drug development team. The members of our development leadership team have served in positions at global pharmaceutical organizations, and importantly, each has also worked productively in resource-constrained environments, such as at start-up biotechnology companies. Key members of our team have also led critical disciplines such as chemistry, ADME & PK, and clinical development of approved products. This set of diverse experiences provides our team not only with the knowledge of how to develop novel product candidates, but the ability to do so in a capital-efficient fashion.

Test our product candidates only in the patients who we believe are most likely to derive benefit. We plan to use biomarkers both to identify the activating molecular alterations that represent the drug targets that we wish to pursue, and to precisely define the patient populations in which we would test those product candidates based on the presence of the biomarkers associated with those specific alterations. 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 receive commercial access to the applicable drugs.

Develop, or pursue relationships with third parties to develop, companion diagnostics to assist in identifying appropriate patients for any product candidates we are able to successfully commercialize. We believe that the availability of high quality companion diagnostics is essential to formalize biomarker discovery and utilization into a platform that can be used by regulators, physicians, payors and, most importantly, patients themselves, to facilitate administration of the applicable therapeutics to the most appropriate patients. A companion diagnostic is a test or measurement that evaluates the presence of biomarkers in a patient, which

information can then assist physicians in selecting the specific drugs or treatments that may be most effective for that patient. With respect to our proposed and potential future product candidates, we believe that any high quality companion diagnostics that we or third parties are able to successfully develop 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.

In-license development candidates that meet our strict criteria. In some instances, the most promising oncogenic activating gene alteration targets that we identify through our analyses may be the subject of a compound already in development with potent activity against the target. In these cases, we may attempt to in-license such compounds if they meet our strict scientific and development criteria, particularly if we believe that their therapeutic potential could be better realized by us. This approach is exemplified by our recent in-license of RXDX-101 and RXDX-102, two investigational agents with potential against the Trk family of tyrosine kinase receptors, targets that we prioritized for development based on our analyses using our Oncolome database.

Seek and maintain commercial rights and, when and if appropriate, establish commercialization and marketing capabilities. We currently have exclusive worldwide commercialization rights to all of our programs in development. We intend, when and if it makes strategic and operational sense, to retain these commercial rights and those for any future product candidates we may pursue on a territory-by-territory basis and establish internal commercialization and marketing capabilities.

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Pipeline

Consistent with our strategy, each of our initial two in-licensed product candidates and each of our three internal discovery programs, for which we hold or have entered into agreements granting us exclusive global marketing rights, is being developed for precise biomarker-defined precise patient groups. Each of our product candidates is in the early stage of development, and we anticipate that it will be several years before any of our product candidates could be commercialized.

We have only recently entered into a license agreement to obtain the rights to RXDX-101 and RXDX-102. That license agreement, entered in October 2013 with NMS, became effective on November 6, 2013. As a result, all discovery-stage, preclinical studies and clinical trials and other development activities relating to those product candidates that were conducted prior to November 6, 2013 were performed by NMS and any third parties with which it contracted. We had no involvement or input in, nor did we have any control over, any of those activities. All of the descriptions of those product candidates in this Annual Report on Form 10-K have been generated based on information provided by NMS or, in some cases, such as the graphic disclosure of preclinical study results for RXDX-101 and RXDX-102, are included in the form provided to us by NMS. NMS has consented to our use of the data it has provided in this Annual Report on Form 10-K.

RXDX-101: Lead Oncology Clinical Asset

RXDX-101 is a new chemical entity that we in-licensed from NMS. RXDX-101 is an orally available, selective tyrosine kinase inhibitor of the Trk family tyrosine kinase receptors (TrkA, TrkB and TrkC), ROS1 and ALK proteins. RXDX-101 is designed as a targeted therapeutic candidate to treat patients with cancers that harbor activating alterations to TrkA, TrkB, TrkC, ROS1 or ALK. Candidate alterations include gene rearrangements or mutations, splice variants, increased gene copy number and increased gene expression.

Rationale for Targeting TrkA, TrkB, TrkC, ROS1 and ALK

About TrkA. The Trk (tropomyosin receptor kinase)/NTRK (neurotrophin tyrosine receptor kinase) family tyrosine kinase receptors, which include TrkA/NTRK1, TrkB/NTRK2 and TrkC/NTRK3, are activated by neurotrophins, a family of nerve growth factors. The Trk family members play a key role in normal central and peripheral neuronal cell development and differentiation. They regulate the survival (or prevention of programmed cell death) and maintain the function of neuronal cells throughout the body. Trk receptors are found on a number of different cell types, and many non-neuronal cells also produce neurotrophins. 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. Oncogenic TrkA translocations (fusion proteins with tropomycin-3) have been reported in colorectal, non small cell lung, or NSCLC, papillary thyroid, pancreatic and certain prostate cancers. The TrkA fusion protein has a constitutively active kinase that provides the driving force for transformation and tumor progression, via the relay of growth and survival signals within cancer cells. In addition, TrkA overexpression and activation of kinase driven signal transduction pathways can be activated by its neural growth factor, or NGF, ligand, produced by tumors or non-tumor cells. The growth and survival of cancers such as ovarian, breast and oral squamous cancers are maintained by TrkA/NGF auto-stimulation and often occur early in the process of tumor formation. Further, in neuroblastomas, a type of extracranial solid cancer, the TrkA splice variant TrkAIII can be produced that switches TrkA to an oncogene, which promotes tumor progression often with a more aggressive character. TrkAIII containing tumors are resistant to chemotherapy-induced cell death, and they induce the formation of new blood vessels, or angiogenesis, to allow the tumors to grow larger and metastasize.

About TrkB. TrkB acts as an oncogene when overexpressed in neuroblastomas and ovarian cancer. TrkB expression can respond to its growth factor ligand, BDNF, produced by tumor cells or non-tumor cells around the tumor, including immune cells such as macrophages. Activated TrkB receptors relay growth and survival signals into the cancer cells and amplify the expression of additional oncogenes such as mycN. Tumors expressing TrkB oncogenes are more aggressive, drug resistant, highly angiogenic and more invasive for establishing metastatic tumors. Studies have shown that patients with TrkB driven tumors have poor survival.

About TrkC. Neurotrophin-3 is the normal growth factor for TrkC. Oncogenic translocations involving TrkC kinase domain generate fusion proteins that have been identified in acute myeloid leukemia, salivary gland carcinoma, adult secretory breast cancer, congenital fibrosarcoma and pediatric nephroma and neuroblastoma. Depending on the tumor type, TrkC expression can accelerate angiogenesis and can be associated with perineural skin invasion (basal cell and cutaneous squamous cell carcinomas) via expression of proteases to break barriers and migration molecules to establish metastatic tumors.

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. Genetic changes in ROS1, such as fusions, rearrangements, mutations or copy number increases, create oncogenes, which can lead to cancer. 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

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survival. ROS1 was first discovered in NSCLC patients in the form of a ROS fusion protein (six different partners for ROS1). Two other genetic rearrangements of ROS1 have been detected in a variety of other cancers, including glioblastoma multiforme, cholangiocarcinoma, ovarian cancer, gastric adenocarcinoma, colorectal cancer, inflammatory myofibroblastic tumor, angiosarcoma and epitheloid hemangioendothelioma.

About ALK (Anaplastic lymphoma kinase). ALK also belongs to the insulin-receptor superfamily and is related to ROS1. ALK was first identified in anaplastic lymphomas, a distinct subset of non-Hodgkin s lymphoma. Molecular changes in ALK through gene rearrangements, mutations, and overexpression lead to the formation of at least 14 ALK oncogenes. 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. In addition to anaplastic lymphomas, ALK oncogenes are found in a number of cancers such as NSCLC, diffuse large B-cell lymphoma, neuroblastomas, inflammatory myofibroblastic tumors and possibly subsets of esophageal/gastric and renal cell cancers. A currently available ALK inhibitor drug, crizotinib, has demonstrated potent *in vitro*, *in vivo* and human anti-tumor activity, validating the utility of ALK inhibitors. However, the rapid emergence of crizotinib-resistant tumors (especially in NSCLC) and the poor penetration of crizotinib into the brain for treating brain metastases support the need for the development of improved ALK inhibitors with better penetration of the blood brain barrier, a separation of circulating blood from the brain and activity against crizotinib-resistant ALK mutations.

Incidence of TrkA, TrkB, TrkC, ROS1 and ALK Mutations; Opportunity for RXDX-101

Research to date indicates that Trk, 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.

TrkA appears to be rearranged across a range of tumor types with a frequency usually in the low single digit percentages. Studies suggest that TrkA is rearranged in ALK mutation negative and epidermal growth factor receptor, or EGFR, mutation negative non small cell lung adenocarcinoma patients, as well as in colorectal adenocarcinoma patients and in papillary thyroid cancer patients.

TrkB and TrkC alterations have been implicated in tumor types including neuroblastoma, secretory breast cancer and non small cell lung cancer, among other tumor types, but the frequency of these alterations is not yet known.

ROS1 appears to be rearranged across a range of tumor types with a frequency usually in the low single digit percentages. Studies suggest that ROS1 is rearranged in non small cell lung adenocarcinoma cancer patients, stomach cancer patients, glioblastoma patients and cholangiocarcinoma patients.

ALK appears to be rearranged across a range of tumor types with a frequency usually in the single digit percentages. Studies suggest that ALK is rearranged in non small cell lung adenocarcinoma cancer patients, neuroblastoma patients and anaplastic large cell lymphoma patients.

The potential ability of RXDX-101 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, and

its observed ability to cross the blood brain barrier in preclinical studies, attracted us to the profile of this product candidate and support the market opportunity for the product.

RXDX-101 Preclinical Data

RXDX-101 is an orally available potent inhibitor of the TrkA, TrkB, TrkC, ROS1 and ALK tyrosine kinases. *In vitro*, RXDX-101 achieves low nanomolar inhibition of TrkA, TrkB, TrkC, ROS1 and ALK. RXDX-101 has been tested *in vivo* in three animal species to date, the mouse, rat and dog. It has demonstrated *in vivo* antitumor activity against various TrkA, ROS1 or ALK-driven mouse xenograft models of different human cancers, has also demonstrated oral bioavailability in all three species tested, and has been observed to efficiently cross the blood brain barrier in all three species tested.

The graphs below depict the results of some of the preclinical studies of RXDX-101 conducted to date. Each of the studies for which results are shown below involved the administration of RXDX-101 orally twice daily for 10 days in mouse xenograft models of various cancers driven by one of the molecular targets of RXDX-101, TrkA, ROS1 or ALK. Each of these studies were conducted by NMS or its third party contractors; we had no involvement in the conduct of these studies and the graphs below were provided by NMS.

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The following graph demonstrates the *in vivo* anti-tumor activity observed with the use of RXDX-101 against a TrkA-driven mouse xenograft model of human colorectal cancer:

The following graph demonstrates the *in vivo* anti-tumor activity observed with the use of RXDX-101 against a ROS1-driven Ba/F3 mouse xenograft model:

The following graph demonstrates the *in vivo* anti-tumor activity observed with the use of RXDX-101 against an ALK-driven mouse xenograft model of human NSCLC:

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The following graph demonstrates the survival benefit observed with the use of RXDX-101 against an ALK-driven mouse xenograft model of brain metastases associated with human NSCLC, which provides support for RXDX-101 s potential ability to cross the blood brain barrier:

Phase I/II Clinical Trial

NMS has filed a Clinical Trial Application under the European Directive to the Italian Competent Authority that enabled NMS to commence a Phase I/II clinical trial in patients with solid tumors that are positive for alterations in TrkA, ROS1 or ALK. This trial, which is currently ongoing at two clinical sites in Italy, is an open label trial that has two phases. The first phase is a Phase I dose escalation phase that will include 20 to 30 patients, depending on when the maximum tolerated dose is achieved, with solid tumors with genetic mutations of TrkA, ROS1 or ALK. The second phase is an expansion phase utilizing the recommended Phase II dose identified in the first phase and is expected to include several cohorts of patients that have alterations to TrkA, ROS1 or ALK. Although we have not yet determined the types of cancer we may study in the second phase of this trial, we currently anticipate that the cohorts will consist of colorectal cancer and NSCLC, among other cancer types.

The primary objectives of the trial are to evaluate the safety and tolerability of RXDX-101 and to determine its maximum tolerated dose when administered to patients with TrkA-, ROS1- or ALK-positive solid tumors.

Secondary objectives of this trial are to:

- determine the process by which RXDX-101 is distributed and metabolized in the body, which is referred to as pharmacokinetics;
- assess the biochemical and physiological effects of RXDX-101 on the human body, which is referred to as pharmacodynamics; and
- evaluate any early evidence of anti-tumor activity in patients with TrkA-, ROS1- or ALK-positive tumors.

The Phase I/II trial is not powered to show results with statistical significance. Statistical significance means that an effect is unlikely to have occurred by chance. Clinical trial results are considered statistically significant when the probability of the results occurring by chance, rather than from the efficacy of the product candidate, is sufficiently low. Since this trial is not powered to show results with statistical significance, the results from the trial may be attributable to chance and not the clinical efficacy of RXDX-101. This trial design is customary for a Phase I and some Phase II clinical trials, the principal purpose of which is to provide the basis for the design of larger, definitive trials that are powered by the addition of more patients to potentially show statistical significance. Pending guidance from regulatory agencies such as the FDA, we would likely design any later stage trials that are intended to support marketing approval applications to show statistical significance. We would do so by enrolling a larger number of patients based on the clinical data observed in earlier trials.

Patients treated with RXDX-101 have experienced some adverse events, which have been predominantly gastrointestinal or constitutional in nature, but there have been no dose limiting toxicities experienced by any of the patients treated with RXDX-101 in this trial to date.

We submitted an investigational new drug application, or IND, with the FDA, to expand the clinical development program to sites in the United States, as well as additional sites in Europe.

RXDX-101 Companion Diagnostic

Several companion diagnostic technologies are available for measuring alterations in TrkA, ROS1 and ALK. There is an FDA-approved fluorescence in situ hybridization, or FISH, test for measuring ALK translocations (Vysis, manufactured by Abbott Molecular). There is also a commercially available FISH test for measuring ROS1 fusion proteins, and we are aware of at least one group that has developed a FISH test for measuring TrkA fusion proteins. TrkA fusion proteins can also be measured by immunohistochemistry, or IHC, using commercially available antibodies. In addition, NMS has developed polymerase chain

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reaction, or PCR, assays for measuring fusion proteins for each of TrkA, TrkB, TrkC, ROS1 and ALK. Finally, several commercial, as well as academic, groups evaluate sequence mutations and translocations of TrkA, TrkB, TrkC, ROS1 and ALK by next generation sequencing. It is our intent to evaluate each of these candidate diagnostic approaches for measuring alterations to TrkA, TrkB, TrkC, ROS1 and ALK and select a technology to be pursued by us or a third-party collaborator, after taking into consideration scientific and commercial factors.

RXDX-102: Preclinical Asset

RXDX-102 is a second new chemical entity that we in-licensed from NMS. RXDX-102 is an orally available, selective inhibitor of the TrkA, TrkB and TrkC proteins. RXDX-102 is designed as an oncogene-targeted therapeutic candidate to treat patients with cancers that harbor activating alterations to TrkA, TrkB or TrkC. Candidate alterations include gene rearrangements or mutations, increased gene copy number and increased gene expression. RXDX-102 is a preclinical product candidate. However, as a result of the preliminary Phase I results relating to RXDX-101 that we have seen to date, we have decided to designate RXDX-102 as a back-up compound to RXDX-101. Accordingly, we will not devote further development resources to RXDX-102 unless the development program for RXDX-101 is unsuccessful.

RXDX-102 Preclinical Data

RXDX-102 is an orally available selective inhibitor of TrkA, TrkB and TrkC. In *in vitro* studies performed to date, RXDX-102 achieves single digit nanomolar inhibition of TrkA, TrkB and TrkC enzymatic assays. RXDX-102 has been tested *in vivo* in four animal species to date, the mouse, rat, dog and primate. It has demonstrated *in vivo* antitumor activity against various TrkA-, TrkB- or TrkC-driven mouse xenograft models of cancer, and has also demonstrated oral bioavailability in all four species tested to date.

The graphs below depict the results of some of the preclinical studies of RXDX-102 conducted to date. Each of the studies for which results are shown below involved the administration of RXDX-102 orally twice daily for 10 days in mouse xenograft models of various cancers driven by one of the molecular targets of RXDX-102, TrkA, TrkB or TrkC. Each of these studies were conducted by NMS or its third party contractors; we had no involvement in the conduct of these studies and the graphs below were provided by NMS.

The following graph demonstrates the *in vivo* anti-tumor activity observed with the use of RXDX-102 against a TrkA-driven mouse xenograft model of human colorectal cancer:

The following graphs demonstrates the *in vivo* anti-tumor activity observed with the use of RXDX-102 against a TrkB-driven Ba/F3 mouse xenograft model and a TrkC-driven Ba/F3 mouse xenograft model:

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RXDX-102 Companion Diagnostic

To the extent that we decide in the future to develop RXDX-102, we would intend to pursue a companion diagnostic strategy for RXDX-102 similar to that described above for RXDX-101 under the heading RXDX-101: Lead Oncology Asset RXDX-101 Companion Diagnostic.

Spark-1 through Spark-6

In our mining of our Oncolome database for molecular alterations that frequently occur in tumor tissue samples to date, we have identified six molecular targets, which, when altered, we believe to drive tumor growth. We refer to these six targets as Spark-1 through Spark-6. The six Spark targets consist of a combination of genetic and epigenetic targets. Although our research and development of these targets is in a very early stage, we believe that activation of these targets, via over-expression or gene rearrangement, may be oncogenic by promoting cell growth and survival in certain tissues. Additionally, though these protein targets are not yet validated, we believe that inhibition of the activated forms of these proteins in cancer-like cells may lead to impaired cell growth or cell death. We have prioritized three of these targets (Spark-1, Spark-2 and Spark-3) and have initiated target validation and small molecule drug discovery activities against some of these targets. Such discovery activities include, or may in the future include, but are not limited to: x-ray crystallography, structure-based drug design, virtual screening, *in vitro* screening, *in vivo* screening, medicinal chemistry and lead optimization. We intend to develop our first IND candidate against one of the Spark-1, Spark-2 or Spark-3 targets by as early as 2015.

License Agreement with NMS

We entered into a license agreement with NMS on October 10, 2013, which was amended on October 25, 2013 and became effective on November 6, 2013, which grants us exclusive global rights to develop and commercialize RXDX-101 and RXDX-102. Our development rights under the license agreement are exclusive for the term of the agreement with respect to RXDX-101 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 RXDX-101 and RXDX-102, and include the right to grant sublicenses. The license agreement provides that we are responsible for all ongoing financial and other requirements of the Phase I/II clinical trial of RXDX-101 and for continued preclinical development of RXDX-102. We are obligated under the license agreement to use commercially reasonable efforts to develop and commercialize a product based on either or both of RXDX-101 or RXDX-102, and, with the exception of the transfer to us without cost of NMS s existing inventory of RXDX-101 and RXDX-102 material, we are responsible for all future development and commercialization costs for RXDX-101 and RXDX-102.

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 provide for an up-front payment to NMS of $7.0 million, and we made a cash payment to NMS for the full amount on November 14, 2013. When and if commercial sales of a product based on either or both of RXDX-101 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 parties to commercialize the product. We are also obligated under the terms of the license agreement to engage NMS to perform services valued at $1.0 million or more between November 6, 2013 and December 31, 2014, which services could include, among others at our election, manufacture and supply services, technology transfer activities, preclinical activities, process development activities and assay development activities. 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. The first such milestone payment is not due until we elect to initiate the first randomized Phase II clinical trial, which, based on our current estimates and certain assumptions, we anticipate could occur as early as 2015.

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 RXDX-101 and RXDX-102.

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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. Additional 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, including chemotherapy, hormone therapy and targeted 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 payors. 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.

RXDX-101

RXDX-101 has demonstrated potent activity in animal testing to date against the five molecular targets, TrkA, TrkB, TrkC, ROS1 and ALK. We may pursue indications in cancers where any one or more of these genes are altered.

We are presently aware of at least the following two compounds that are currently in clinical development and may have activity against Trk receptor activating alterations: Daiichi Sankyo and its subsidiary Plexxikon s PLX-7486, which is reported to have activity against Trk and other molecular targets and which we currently believe to be in a Phase I clinical study, based on publicly available information published by the National Institutes of Health and updated as of September 2013; and Tesaro, Inc. s TSR-011, which is reported to have activity against Trk and other molecular targets and which we currently believe to be in a Phase I/II clinical trial, based on information published by the National Institutes of Health and updated as of January 2014. We believe that other pharmaceutical companies may be seeking to develop Trk receptor selective inhibitors that may enter clinical development before or during a similar timeframe as RXDX-101.

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We also believe that other pharmaceutical companies may be seeking to develop ROS1 selective inhibitors, and are aware of several such products currently in clinical development by other companies.

Xalkori® is the only drug currently approved in the United States to treat ALK-mutant NSCLC. In addition, we are aware of several products in clinical development targeting cancer-causing mutant forms of ALK for the treatment of NSCLC patients, some of which are more advanced in clinical development than RXDX-101. We believe RXDX-101 potentially offers several important advantages over Xalkori, including potentially superior efficacy due to activity against certain ALK-resistant mutations, as well as potentially increased ability to cross the blood brain barrier, therefore offering an opportunity for clinical activity against brain metastases that are common in ALK mutant NSCLC.

RXDX-102

RXDX-102 has demonstrated potent activity in animal models against three molecular targets, TrkA, TrkB and TrkC.

We are presently aware of the two compounds described above under the heading RXDX-101 that are currently in clinical development and may have activity against Trk activating alterations.

Spark-1, Spark-2 and Spark-3

Spark-1, Spark-2 and Spark-3 represent activating gene alterations that we believe drives cancer biology in certain tumors. To our knowledge, there are no commercial entities actively developing clinical-stage drugs directed specifically to any of these three targets. We believe that other pharmaceutical companies may seek to develop selective inhibitors against the Spark-1, Spark-2 or Spark-3 targets and that these potential inhibitors may enter clinical development before or during a similar timeframe as the compounds that we intend to develop against one or more of these three targets.

Commercialization

We have not yet established a sales, marketing or product distribution infrastructure because our lead candidates are still in discovery, preclinical or early clinical development. We anticipate that we will retain commercial rights in the United States for any of our product candidates for which we may in the future receive marketing approvals. We currently anticipate that, when appropriate, we will seek to access the United States oncology market through a focused, specialized, internal sales force.

Subject to receiving marketing approvals, we expect to commence commercialization activities by building a focused internal sales and marketing team in the United States to sell our products. We believe that such an approach will enable us to address the community of oncologists who are the key specialists in treating the patient populations for which our current product candidates are being developed. Outside the United States, we may enter into distribution and other marketing arrangements with third parties for any of our product candidates that obtain marketing approval in foreign jurisdictions.

We also plan to build a marketing and sales management force to create and implement marketing strategies for any products that we may in the future market through our own sales teams and to oversee and support our sales force. We anticipate that our goals for any such marketing force include developing educational initiatives with respect to any approved products and establishing relationships with thought leaders in relevant fields of medicine.

We currently expect that any third parties with which we may collaborate in the future on the development of any commercial companion diagnostics for use with our therapeutic products 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