

Ignyta, Inc.  
 Form 424B4  
 March 14, 2014  
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**Filed Pursuant To Rule 424(b)(4)  
 File Nos. 333-194241 and 333-194549**

**PROSPECTUS**

**5,245,000 Shares**

**Common Stock**

We are offering 5,245,000 shares of our common stock.

Our common stock is quoted on the OTCQB Marketplace and the OTC Bulletin Board under the symbol RXDX. On March 13, 2014, the last reported sale price for our common stock as reported on the OTCQB Marketplace was \$9.95 per share. Our common stock has been approved for listing on the NASDAQ Capital Market under the symbol RXDX, beginning on March 14, 2014.

**Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page 8 of this prospectus for a discussion of factors you should consider before buying shares of our common stock.**

*We are an emerging growth company as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.*

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

	<b>Per Share</b>	<b>Total</b>
Public offering price	\$ 9.150	\$ 47,991,750
Underwriting discounts and commissions <sup>(1)</sup>	\$ 0.549	\$ 2,879,505
Proceeds, before expenses, to us.	\$ 8.601	\$ 45,112,245

(1) Please refer to Underwriting on beginning on page 127 of this prospectus for additional information regarding underwriting compensation.

We have granted the underwriters an option for 30 days to purchase up to 786,750 additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$3,311,431, and the total proceeds to us, before expenses, will be \$51,879,082.

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Delivery of the shares of common stock will be made on or about March 19, 2014.

**Leerink Partners**

**Ladenburg Thalmann & Co.**

**The date of this prospectus is March 13, 2014**

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**About This Prospectus**

You should rely only on the information that we have provided or incorporated by reference in this prospectus. We have not authorized anyone to provide you with different information. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained in this prospectus. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus is accurate only as of the date on the front of this document and that any information we have incorporated by reference is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, or any sale of a security registered under the registration statement of which this prospectus is a part.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or

will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading **Where You Can Find Additional Information**.

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As used in this prospectus, 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 prospectus have been adjusted to give effect to those reverse stock splits.

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 prospectus 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.

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**PROSPECTUS SUMMARY**

*This summary does not contain all of the information that should be considered before investing in our common stock. Investors should carefully read this prospectus, and the registration statement of which this prospectus is a part, in their entirety before investing in our common stock, including the information discussed under Risk Factors in this prospectus.*

**Our Company**

**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. We have entered into a license agreement with Nerviano Medical Sciences S.r.l., or NMS, granting us exclusive global development and marketing rights to RXDX-101 and RXDX-102, which became effective on November 6, 2013. We also have three discovery stage programs, Spark-1, Spark-2 and Spark-3, directed to emerging oncology targets identified through mining of our database of information from proprietary and publicly available tumor samples, called Oncolome.

Our business is 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 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. Our strategy is to leverage the biomarker insights that we gain through our genetic and epigenetic mining of our Oncolome database and the knowledge of cancer biology of our management and drug discovery team, with the goal of discovering or acquiring, validating, developing and commercializing a pipeline of novel product candidates for the treatment of cancer.



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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.

For more information regarding our business, see the disclosure under the headings "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business" included elsewhere in this prospectus.

## **Our 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.

Apply a multi-omics approach to discover activating molecular alterations that drive cancer biology.

Leverage deep cancer biology expertise and systems biology understanding to identify the specific role of activating alterations.

Deploy drug design tools to develop small molecule inhibitors of activating targets.

Employ a capital-efficient drug development team.

Test our product candidates only in the patients that we believe are most likely to derive benefit.

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.

In-license development candidates that meet our strict criteria.



Seek and maintain commercial rights and, when and if appropriate, establish commercialization and marketing capabilities.

**Risks Associated with Our Business**

Our business and ability to execute our business strategy are subject to a number of risks of which you should be aware before you decide to buy our common stock. In particular, you should consider the following risks, which are discussed more fully in the section entitled "Risk Factors" in this prospectus, as well as the other risks described in "Risk Factors."

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 revenue to date and may never generate revenue or achieve profitability.

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We will need substantial additional funding to continue our operations, which could result in significant 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, reduce or eliminate our product development programs or commercialization efforts and could cause our business to fail.

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

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

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

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.

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.

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.

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

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.

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 market and our business would be harmed.

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

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

There is not now, and there may never be, an active, liquid and orderly trading market for our common stock, which may make it difficult for you to sell your shares of our common stock.

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

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

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.

**Corporate Information**

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. and 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 Securities and Exchange Commission, or 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. Our principal executive offices are located at 11095 Flintkote Avenue, Suite D, San Diego, California 92121, and the telephone number at our principal executive office is (858) 255-5959. Our website address is <http://www.ignyta.com>. We have not incorporated by reference into this prospectus the information on our website, and you should not consider it to be a part of this document.

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012. 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 of 1933, as amended, or 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 refer to the Jumpstart Our Business Startups Act of 2012 herein as the JOBS Act, and references herein to emerging growth company have the meaning associated with it in the JOBS Act. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from specified disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include:

being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced Management's Discussion and Analysis of Financial Condition and Results of Operations disclosure;

not being required to comply with the requirement of auditor attestation of our internal controls over financial reporting;

not being required to comply with 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 the financial statements;

reduced disclosure obligations regarding executive compensation; and

not being required to hold a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved.

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For as long as we continue to be an emerging growth company, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of that classification. We have taken advantage of certain of reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock.

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.

We are also a smaller reporting company as defined in Rule 12b-2 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and have elected to take advantage of certain of the scaled disclosure available for smaller reporting companies.

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**The Offering**

Common stock offered by us	5,245,000 shares
Common stock to be outstanding after this offering	19,179,876 shares
Option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to 786,750 additional shares of our common stock.
Use of proceeds	We estimate that the net proceeds from this offering will be approximately \$44.5 million, or approximately \$51.3 million if the underwriters exercise their option to purchase additional shares in full, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We intend to use the net proceeds of this offering to fund the development of our lead product candidate, RXDX-101, and for other research and development of our other product candidates, working capital and general corporate purposes. See Use of Proceeds for a more complete description of the intended use of proceeds from this offering.
Risk factors	Investing in our securities involves a high degree of risk and purchasers may lose their entire investment. You should read the Risk Factors section of this prospectus for a discussion of certain factors to consider carefully before deciding to purchase any shares of our common stock.
NASDAQ Capital Market symbol	RXDX

The number of shares of our common stock to be outstanding after this offering is based on 13,934,876 shares of common stock outstanding as of December 31, 2013, and excludes:

1,133,153 shares of common stock issuable upon the exercise of outstanding stock options as of December 31, 2013, at a weighted average exercise price of \$4.33 per share;

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41,668 shares of common stock issuable upon the exercise of outstanding warrants as of December 31, 2013, at a weighted average exercise price of \$4.20 per share;

1,567,209 shares of common stock reserved for future issuance under our Amended and Restated 2011 Stock Incentive Plan, or the Ignyta Plan, as of December 31, 2013; and

the exercise by us of a contractual right to repurchase 400,000 shares of restricted common stock in February 2014 in connection with the departure of an employee.

Unless otherwise indicated, all information contained in this prospectus, and the number of shares of common stock outstanding as of December 31, 2013, assumes no exercise by the underwriters of their option to purchase up to an additional 786,750 shares of our common stock.



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The following tables summarize our consolidated financial data for the periods presented and should be read together with the sections of this prospectus entitled Risk Factors, Selected Consolidated Financial Data and Management's Discussion and Analysis of Financial Condition and Results of Operations, as well as our consolidated financial statements and related notes appearing elsewhere in this prospectus. We derived the summary statement of operations data for the years ended December 31, 2012 and 2013 from our audited consolidated financial statements and related notes appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of the results we expect in the future.

	<b>Year Ended December 31,</b>	
	<b>2013</b>	<b>2012</b>
	<b>(audited)</b>	
<b>Consolidated Statements of Operations Data:</b>		
<b>Revenue</b>	\$	\$
<b>Expenses</b>		
Research and development	10,170,866	708,043
General and administrative	3,730,941	547,882
<b>Loss from operations</b>	(13,901,807)	(1,255,925)
<b>Other expense</b>	(309,741)	(22,619)
Loss before income taxes	(14,211,548)	(1,278,544)
Income tax provision	2,095	1,308
<b>Net loss</b>	\$ (14,213,643)	\$ (1,279,852)
Basic and diluted loss per share of common stock	\$ (3.83)	\$ (2.00)
Weighted average number shares outstanding	3,711,885	640,364

The unaudited pro forma balance sheet data set forth below give effect to our issuance and sale of 5,245,000 shares of our common stock in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

	<b>As of December 31, 2013</b>	
	<b>Actual</b>	<b>Pro Forma</b>
	<b>(audited)</b>	<b>(unaudited)</b>
<b>Consolidated Balance Sheet Data:</b>		
Cash and cash equivalents	\$ 51,803,716	\$ 96,290,961
Total assets	53,318,840	97,806,085
Total liabilities	11,531,235	11,531,235
Deficit accumulated during the development stage	(15,572,940)	(15,572,940)

Total stockholders' equity	41,787,605	86,274,850
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**RISK FACTORS**

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with the other information contained in this prospectus, including our consolidated financial statements and the related notes, before making any decision to invest in shares of our common stock. This prospectus contains forward-looking statements. If any of the events discussed in the risk factors below occurs, our business, prospects, results of operations, financial condition and cash flows could be materially harmed. If that were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks not currently known to us or other factors not perceived by us to present significant risks to our business at this time also may impair our business 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 revenue to date and may never generate revenue or achieve profitability.*

We are a development-stage biopharmaceutical company with a limited operating history. We have not generated any 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, 2013 was \$14.2 million. As of December 31, 2013, we had an accumulated deficit of \$15.6 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 primarily on the development of RXDX-101, Spark-1, Spark-2 and Spark-3, which we believe will result in our continued incurrence of significant research and development and other expenses related to those programs. If the clinical trials for any of our products fail or produce unsuccessful results and those product candidates do not gain regulatory approval, or if any of our product candidates, if approved, fail 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 will need substantial additional funding to continue our operations, which could result in significant 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, reduce or eliminate 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 the clinical development of our product candidates 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.

On November 6, 2013, we closed a private placement of our common stock for gross proceeds to us of approximately \$46.4 million, and on November 29, 2013, we closed a subsequent private placement of our common stock for gross proceeds to us of approximately \$7.6 million. In addition, on December 31, 2013, we received aggregate funding of \$10 million, representing the full principal amount under a loan from Silicon Valley Bank, or SVB. Even after giving effect to the proceeds received from the private placements, the loan from SVB and the proceeds of this offering, we will require additional capital for the further development and commercialization of our product candidates and may need to raise additional funds sooner than we currently anticipate if we choose to and are able to expand more rapidly

than we currently anticipate. Further, we expect our expenses to increase in connection with our ongoing activities, particularly as we continue the ongoing

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development of RXDX-101 and other product candidates. 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 operating as a public company. 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 will need to obtain substantial additional funding in order to continue our operations.

To date, we have financed our operations entirely through equity investments by founders and other investors 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. For instance, in connection with the closing of the private placements on November 6, 2013 and November 29, 2013, we issued an aggregate of 9,010,238 shares of our common stock, which equaled approximately 66.62% of our issued and outstanding capital stock as of February 28, 2014. If we raise additional capital through the incurrence of further indebtedness, as we have done with our loan from SVB and 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 product.

If we are unable to raise capital when needed or on attractive terms, we could be forced to delay, reduce or eliminate our research and development programs or any future commercialization efforts. Any of these events could significantly harm our business, financial condition 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.***

Our initial focus was on the discovery and development of biomarkers and molecular and companion diagnostic tests for certain autoimmune diseases. Only since May 2013 have we focused our business on precision medicines for the treatment of cancers. Consequently, we have limited experience operating this business and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. Further, the early stage nature of our business results in a limited operating history upon which you can evaluate our business and prospects. Our lead product candidates are in the earliest stages of development, have not obtained regulatory marketing approval, have never generated any sales and will 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 using unproven technologies;

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

engage corporate partners to assist in developing, testing, manufacturing and marketing our product candidates;

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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;

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

maintain, grow and manage our internal teams as and to the extent we increase our operations and develop new segments of our business;

develop and maintain successful collaboration, strategic and other relationships for the development and commercialization of our product candidates and those of our partners that receive regulatory approvals; 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 develop product candidates, raise capital, expand our business or continue our operations.

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

On December 31, 2013, we incurred \$10 million of indebtedness at an interest rate of 6.92% under an amended and restated loan agreement with SVB. We are obligated to make payments under the loan agreement in 36 equal monthly installments following a 12-month period of interest-only payments, and we expect our interest payment obligations thereunder to total approximately \$644,000 for our 2014 fiscal year. Further, the terms of the loan agreement require that we make a final lump-sum payment of \$1,050,000, equal to 10.5% of the principal amount of the loan thereunder, upon the maturity date of such loan on December 1, 2017. 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 SVB certain financial and insurance information and comply with certain notice requirements, and covenants that restrict our ability, without SVB's prior consent, to: replace our chief executive officer; 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 under the loan agreement. In the event of any such default, SVB may be able to declare all borrowed funds, together with accrued and unpaid interest, immediately due and payable, thereby potentially causing all 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.



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**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 Chief Scientific Officer recently resigned from his positions with us.***

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, our President, Chief Executive Officer and Chairman of the Board, whose services are critical to the successful implementation of our product candidate development and regulatory strategies. Further, as our approach is built in part upon the drug discovery and development experience of our scientific drug hunter team, which we believe is a significant contributor to our competitive advantage, we are dependent on the maintenance and growth of that team with qualified members containing high levels of expertise in specific scientific fields.

In January 2014, Patrick O Connor, who had been on a medical leave of absence since September 2, 2013, informed us that the state of his health would not allow him to return to his positions as our Senior Vice President, Research, and Chief Scientific Officer, and he resigned from employment with us effective February 5, 2014. Dr. O Connor joined us in May 2013 after Ignyta Operating acquired Actagene, a discovery stage precision medicine company that Dr. O Connor founded in February 2013. Prior to that, Dr. O Connor had served as the chief scientific officer or in comparable positions for several public and private biotechnology companies and assisted in the development of several U.S. Food and Drug Administration, or FDA, approved drugs. Dr. O Connor was a valuable member of our scientific and drug discovery team, and his departure could cause our operations and prospects to suffer.

Except as described in the preceding paragraph, 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. Additionally, several members of our scientific team are consultants rather than employees, and could terminate their consulting relationship with us at any time or with short notice, depending on the terms of their respective consulting agreements with us. 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 as an early-stage company. 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, with contractual provisions and

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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.

On June 19, 2013, we received a letter from legal counsel for Ruga Corporation, a private oncology biopharmaceutical company for which some of our current employees and consultants previously provided services, making certain allegations regarding use of its proprietary synthetic lethal screening technology and certain related claims. We investigated each of those claims and we believe them to be wholly without merit. On August 15, 2013, we responded to the letter from Ruga Corporation's legal counsel, describing the results of our investigation and denying each claim made. We subsequently provided certain information to Ruga Corporation's legal counsel, who has not responded to us. We have received no communication from Ruga Corporation or its counsel since September 26, 2013. We would vigorously defend any claims that may be pursued relating to this matter.

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 European Medicines Agency, or 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 and abuse laws and regulations as they may become applicable to our operations, 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 Discovery and Development of Our Product Candidates**

***We are heavily dependent on the success of our lead product candidate, 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 two product candidates from NMS. Our future success is substantially dependent on our ability to successfully develop, obtain regulatory approval for, and then successfully commercialize RXDX-101, with RXDX-102 as a back-up compound in case the development of RXDX-101 is not successful. Our business depends entirely on the successful development, clinical testing and commercialization of these and any other product candidates we may seek to develop in the future, which may never

occur.

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Before we could generate any revenues from sales of our lead 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 additional clinical development;

manage clinical, preclinical and manufacturing activities;

achieve regulatory approval in multiple jurisdictions;

establish manufacturing relationships for the supply of the applicable product candidate;

build a commercial sales and marketing team, if we choose to market any such product ourselves;

develop and implement marketing 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 the ongoing RXDX-101 Phase I/II clinical trial are not successful, we may not be able to use those results as the basis for advancing the product candidate 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 this product candidate is not justified and may decide to discontinue the program. Clinical testing of RXDX-102 would not commence unless the development of RXDX-101 is not successful, but the results of any future preclinical studies or clinical trials of RXDX-102, if unsuccessful, could lead to our abandonment of the development of that product candidate as well. If studies of these product candidates produce unsuccessful results and we are forced or elect to cease their development, our business and prospects would be substantially harmed.

***Preclinical and clinical testing of our lead 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 licensed the rights to develop our two product candidates from NMS, and the development of those product candidates prior to our license was conducted wholly by NMS or any third parties with which it had contracted. As a result, we were not involved with nor did we have any control over any of those development activities. We have only recently assumed full control of preclinical studies and clinical trials relating to those product candidates. However, because we had no input on NMS's development activities relating to these product candidates prior to us assuming full control, we may discover that all or certain elements of the trials and studies it has previously performed have not been in compliance with applicable regulatory standards or have otherwise been deficient. For

instance, the development of each of these product candidates to date has been conducted only in Europe. As a result, although we may find that those studies meet the standards of applicable European regulatory bodies, the structure and design of those clinical trials and preclinical studies may not meet applicable FDA standards to allow immediate further development of those product candidates in the United States, and also may not meet the standards of applicable regulatory authorities in any non-European foreign country in which we desire to pursue marketing approval for these product candidates. If the studies conducted to date have not been in full compliance with applicable regulatory standards or are otherwise not eligible for continued development in the United States, 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 would 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.

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***Our research and development is based on a rapidly evolving area of science, and our approach to drug discovery and 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 discovery 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. Although epigenetic regulation of gene expression plays an essential role in biological function, very few drugs premised on epigenetics have been discovered. Moreover, drugs based on an epigenetic mechanism that have received marketing approval are not targeted to differentially methylated genes, which is the focus of some of our epigenetic research and development. As a result, identifying drug targets based in part on differential gene methylation may not lead to the discovery or development of any drugs that successfully treat patients with molecularly defined cancers. 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 genetically and epigenetically altered 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 genetically or epigenetically altered cancer drug targets, we may not be able to develop product candidates that are safe and effective inhibitors of all or 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 initial clinical trials. For example, although the preclinical and early clinical results for our lead product candidate has been positive, those results and the results that may be generated in the ongoing Phase I/II clinical trial for RXDX-101 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 is a clinical trial ongoing for RXDX-101, 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;

reaching agreement on acceptable 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;



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

enrolling suitable patients to participate in a trial;

developing and validating companion diagnostics on a timely basis;

changes in dosing or administration regimens;

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

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

regulators instituting a clinical hold due to observed safety findings;

adding new clinical trial sites; or

manufacturing sufficient quantities of product candidate for use in clinical trials.

We currently rely, and we expect to continue to rely, on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. Although we have an agreement in place with a CRO governing its committed activities and conduct, and we expect we will have similar agreements with other CROs 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 CRO'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 future CRO'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 Safety Monitoring Board for the trial, if applicable, or by the FDA, EMA 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 site by the FDA, EMA 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 focused on patients with molecularly defined cancers, 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. In addition, some of our competitors have ongoing clinical trials for product candidates that treat the same indications 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.

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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 alteration we are seeking to target in the applicable trial;

the eligibility criteria for the study in question;

the perceived risks and benefits of the product candidate under study;

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; and

the proximity and availability of clinical trial sites for prospective patients.

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 may 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 trial.

Consistent with our general product development strategy, we intend to design the Phase II aspect of the ongoing Phase I/II clinical trial of RXDX-101 and any future trials for those or other product candidates to include some patients with the applicable molecular alteration that causes the disease, 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 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 a New Drug Application, or 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;

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;

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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 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, RXDX-101 or any other product candidates we may seek to develop in the future, 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 would 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 market and 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 a label that does not include the labeling 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.

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***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 an approved label, or result in significant negative consequences following marketing approval, if any.***

To date, patients treated with RXDX-101 have experienced some drug-related adverse events, which have been predominantly gastrointestinal or constitutional in nature. Results of our trials for our other product candidates could reveal a high and unacceptable severity and frequency of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA, EMA 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 enrolled patients to complete the trial, or result in potential product liability claims. Any of these occurrences may 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 on the product's label;

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 candidate, 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 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 our product candidates. 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. 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, which could negatively affect our development efforts with respect to our drug product candidates and materially harm our business, operations and prospects.

Companion diagnostics are subject to regulation by the FDA and comparable foreign regulatory authorities as medical devices and may 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



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may partner in the future to develop and obtain clearance or approval for these companion diagnostics. We and our potential future collaborators may encounter difficulties in developing and obtaining clearance or approval for these companion diagnostics, including issues relating to the selectivity and/or specificity of the diagnostic, analytical validation, reproducibility, or clinical validation. 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, the 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.***

Because we have limited financial and managerial resources, we must focus our efforts on particular research programs and 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 improperly 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 which we seek it, 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 except in limited situations.

We expect that we may in the future pursue orphan drug designations for at least some of our product candidates. However, obtaining an orphan drug designation can be difficult and we may not be successful in doing so for any of our product candidates. Even if we were to obtain orphan drug exclusivity for a product candidate, that exclusivity may not effectively protect the product from the competition of different drugs for the same condition, which could be approved during the exclusivity period. Additionally, after an orphan drug is approved, the FDA could subsequently approve another application for the same drug for the same condition 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 we may develop for the treatment of rare cancers, and/or the inability to

maintain that designation for the duration of the applicable

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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.

***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 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 some of our product candidates. The Food and Drug Administration Safety and Innovation Act established the new 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 on a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical endpoint, 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.

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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 IV or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or 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.

## **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 CRO we have engaged to continue the Phase I/II clinical trial for RXDX-101, 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, EMA 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 a clinical trial 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. 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, nonclinical 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 effected product candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

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***We plan to rely completely 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.***

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 completely on third-party manufacturers for those services. We presently have only a limited supply of RXDX-101 and RXDX-102, which NMS agreed to provide to us in connection with our recent in-licensing of the rights to develop those product candidates. We have recently entered into a short term supply agreement with NMS to provide us with additional RXDX-101 clinical supply. We also are evaluating NMS and other third-party manufacturers for long-term supply of RXDX-101. We do not currently have any long-term supply commitments in place. We also do not currently have arrangements in place for redundant supply of bulk drug substance. We 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 our product candidates for 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 will not control the manufacturing process of, and will 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. In addition, we expect to have no control over the ability of our contract manufacturers to maintain adequate compliance with cGMPs. If any of our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA, EMA 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. Any such failure by any of our contract manufacturers would significantly impact our ability 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 clinical trials. We do not have, nor do we expect to enter, any agreements for the commercial 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 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



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post-marketing testing, including Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA, EMA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event 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, registration, as well as continued compliance with cGMPs and GCPs for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events 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, complete withdrawal of the product from the market or product recalls;

fines, warning 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.

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. 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.

***We currently have no marketing and 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 do not have a marketing or 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 our product candidates receive regulatory approval, we intend to establish an internal sales and marketing team with technical expertise and supporting distribution capabilities to commercialize our product candidates, which will be expensive and time consuming and will require significant attention of our executive officers to manage. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of any of our products that we obtain approval to market. With respect to the commercialization of all or certain of our product candidates, we may 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. If we are unable to enter into such arrangements when needed on acceptable terms or at all, we may not be able to successfully commercialize any of our product candidates that receive regulatory approval or any such commercialization may experience delays or limitations. 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.

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

Even if we obtain regulatory approval for our product candidates, the products may not gain market acceptance among physicians, health care payors, 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;

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 alteration that our product targets;

acceptance of the drug as a safe and effective treatment by physicians, major operators of 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 payors 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, the 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.

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With respect to our lead product candidate, we are aware of one agent that has been approved by the FDA for ALK-positive NSCLC, which is Pfizer's Xalkor®/crizotinib, and we are aware of several other products in development targeting TrkA, TrkB, TrkC, ROS1 and/or ALK for the treatment of cancer, some of which may be in a more advanced stage of development than RXDX-101. 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 RXDX-101.

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. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in certain of our competitors. As a result, 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. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA, EMA or other regulatory approval, 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.

***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 products for which we obtain marketing approvals.***

There is significant uncertainty related to the third-party coverage and reimbursement of newly approved drugs. 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 payors for any of our product candidates, 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 payors decide which drugs they will pay for and establish reimbursement levels for them, and obtaining coverage and reimbursement approval for a product from any such third-party payor 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, if any. As a result, any denial of private or government payor coverage or inadequate reimbursement for use of our product candidates, if any are commercialized, could harm our business and reduce our prospects for generating revenue.

Further, 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



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other payors of healthcare services 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 products that obtain marketing approval, which may adversely affect our future profitability.

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.

***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 and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our product candidates, 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;

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 clinical trial activity as a result of our assumption



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of control of the RXDX-101 clinical trials currently being conducted in Italy. We may wish to obtain additional such insurance covering studies or trials in other countries should we seek to expand those clinical trials or commence new clinical trials in other jurisdictions or increase the number of patients in any clinical trials we may pursue. 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. If we do not obtain or retain sufficient product liability insurance, we could be responsible for some or all of the financial costs associated with a product liability claim relating to our preclinical and clinical development 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 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 RXDX-101 and RXDX-102. As a result, our current business plans are dependent upon our satisfaction of certain conditions to the maintenance of that agreement and the rights we license under it. The license agreement provides that we are subject to diligence obligations relating to the commercialization and development of a product based on either or both of RXDX-101 or RXDX-102, milestone payments, royalty payments and other obligations. In addition to our license agreement with NMS, 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 our license agreement with NMS, or any future license agreement we may enter on which our business or product candidates are dependent, NMS or other licensors may have the right to 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, including, with respect to our license agreement with NMS, RXDX-101 and RXDX-102. The loss of the rights licensed to us under our license agreement with NMS, 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 market 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. 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.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. 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 validity, enforceability or scope of any issued patents we own or license or any applications that may issue as patents in the future, which may result in those patents being narrowed, invalidated or held unenforceable. 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. If the breadth or strength of protection provided by the

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patents we hold or pursue is threatened, our ability to 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 that obtain regulatory approval would be reduced. Since patent applications 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 that we are the first to file any patent application related to our product candidates.

The license agreement with NMS grants us an exclusive, worldwide license under a portfolio of patents and patent applications directed to the RXDX-101 and RXDX-102 composition of matter, which begin to expire in 2029 for the patents and applications relating to RXDX-101 and in 2028 for the patents and applications relating to RXDX-102. 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 either RXDX-101 or RXDX-102, 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, because filing, prosecuting and enforcing patents in multiple jurisdictions can be expensive, we may elect to pursue patent protection relating to our product candidates in only 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.

In addition to the protection afforded by patents, we seek to rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes 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. 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 prevent material disclosure of the trade secret intellectual property related to our technologies to third parties, we may not be able to establish or maintain the competitive advantage that we believe is provided by such intellectual property, which could materially 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 discovery and development efforts.***

Our research, development and commercialization activities, as well as any product candidates or products resulting from those activities, may infringe or be accused of infringing 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 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 may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes one or more claims of these patents. If our activities or product candidates 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 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.

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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 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. Further, if we were to seek a license from the third party holder of any applicable intellectual property rights, we may not be able to obtain the applicable license rights when needed or on commercially reasonable terms, or at all. The occurrence of any of the above events could prevent us from continuing to develop and commercialize one or more of our product candidates and our business could materially suffer.

***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 of our product candidates, in which case we would need to obtain a license from that third party or develop a different formulation of the product that does not infringe upon the applicable intellectual property, which may not be possible. Additionally, we may identify product candidates that we believe are promising and whose development and other intellectual property rights are held by third parties. In such a case, we may desire to seek a license to pursue the development of those product candidates, as we have done with RXDX-101 and RXDX-102. 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 any patents covering product candidates we may in-license from third-party owners, there may be instances when platform technology patents that cover our product candidates remain controlled by our licensors. For instance, NMS has retained certain patent prosecution rights under our license agreement relating to RXDX-101 and RXDX-102. If any of our current or future licensing partners that retain the right to prosecute patents covering the product candidates we license from them fail to appropriately 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 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. 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 and distract management. If we pursue any litigation, a court may decide that a patent of ours or our licensor's is not valid 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 infringement litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable, or interpreted narrowly and could put our patent applications at risk of not issuing, which could limit our ability to exclude competitors from directly competing with us in the applicable jurisdictions.



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Interference proceedings provoked by third parties or brought by the United States Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome 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 or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

***If we are unsuccessful in obtaining or maintaining patent protection for intellectual property in development, our business and competitive position would be harmed.***

We are seeking patent protection for some of our technology and product candidates. Patent prosecution is a challenging process and is not assured of success. If we are unable to secure patent protection for our technology and product candidates, our business may be adversely impacted.

In addition, issued patents and pending international applications require regular maintenance. 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 unenforceable or by prematurely terminating pending international applications.

***If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.***

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

## **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, 2014, we had 17 employees, 15 of whom were full-time and two of whom were part-time. 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. Future growth would impose significant added responsibilities on members of management, including:

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

effectively managing our discovery research and preclinical development;



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

effectively managing our internal development efforts;

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

developing and managing new divisions of our internal business, including any sales and marketing segment we 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 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 may 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. In addition, we may be subject to federal and state patient privacy regulations, such as the federal Health Insurance Portability and Accountability Act of 1996. 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 and 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

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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.

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 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 the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary and/or our November 2013 private placements of our common stock and may experience one or more ownership changes as a result of this offering or future transactions in our stock, and 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, 2013, we had federal and state net operating loss carryforwards of approximately \$7.3 million that could be limited if the merger or the private placements is an ownership change, or if we experience any other ownership change, which could potentially result in increased future tax liability to us.

***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 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 do not carry any 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 could cause our business to materially suffer.

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**Risks Related to Ownership of our Common Stock and this Offering**

*There is not now, and there may never be, an active, liquid and orderly trading market for our common stock, which may make it difficult for you to sell your shares of our common stock.*

There is not now, nor has there been since our inception, any significant volume of trading activity in our common stock or an active market for shares of our common stock, and an active trading market for our shares may never develop or be sustained after this offering. As a result, investors in our common stock must bear the economic risk of holding those shares for an indefinite period of time. Although our common stock has been quoted on the OTCQB Marketplace, or OTCQB, and OTC Bulletin Board, or OTCBB, over-the-counter quotation systems, trading of our common stock on such systems only recently commenced and has been extremely limited and sporadic and at very low volumes. In connection with this offering, our common stock has been approved for listing on the NASDAQ Capital Market beginning on March 14, 2014, but an active trading market for our common stock may never develop or be sustained. If an active market for our common stock does not develop, it may be difficult for you to sell the shares you purchase in this offering without depressing the market price for the shares or at all. Further, an unestablished trading market for our common stock may also impair our ability to raise capital by selling additional equity in the 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 quoted prices for our common stock currently are, and are 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. In addition to the factors discussed in this Risk Factors section and elsewhere in this prospectus, these factors include:

the product candidates we seek to 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;

actual or anticipated adverse results or delays in our clinical trials;

our failure to commercialize our product candidates, if approved;

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 protection for our product candidates;

our dependence on third parties, including CROs as well as our potential partners that produce companion diagnostic products;

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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;

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;

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, including those described in these Risk Factors, could have a dramatic and material adverse impact on the market price of our common stock.

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

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operat