

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.

	Per Share	Total
Public offering price	\$ 9.150	\$ 47,991,750
Underwriting discounts and commissions ⁽¹⁾	\$ 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.

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.

	Year Ended December 31,	
	2013	2012
	(audited)	
Consolidated Statements of Operations Data:		
Revenue	\$	\$
Expenses		
Research and development	10,170,866	708,043
General and administrative	3,730,941	547,882
Loss from operations	(13,901,807)	(1,255,925)
Other expense	(309,741)	(22,619)
Loss before income taxes	(14,211,548)	(1,278,544)
Income tax provision	2,095	1,308
Net loss	\$ (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.

	As of December 31, 2013	
	Actual	Pro Forma
	(audited)	(unaudited)
Consolidated Balance Sheet Data:		
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 agree