

Ignyta, Inc.
Form POS AM
March 27, 2014
Table of Contents

As filed with the Securities and Exchange Commission on March 27, 2014

No. 333-192956

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

POST EFFECTIVE AMENDMENT NO. 1

TO

FORM S-1

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

IGNYTA, INC.

(Exact name of registrant as specified in its charter)

Nevada
(State of Incorporation)

2834
*(Primary Standard Industrial Classification
Code Number)*
11095 Flintkote Avenue, Suite D

59-3564984
(IRS Employer Identification No.)

San Diego, California 92121

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Edgar Filing: Ignyta, Inc. - Form POS AM

Jonathan E. Lim, M.D.

President and Chief Executive Officer

11095 Flintkote Avenue, Suite D

San Diego, California 92121

(858) 255-5959

(Name, address, including zip code, and telephone number, including, area code, of agent for service)

Copies to:

Cheston J. Larson, Esq.

Matthew T. Bush, Esq.

Matthew W. Grant, Esq.

Latham & Watkins LLP

12670 High Bluff Drive

San Diego, California 92130

(858) 523-5400

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

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

Edgar Filing: Ignyta, Inc. - Form POS AM

Large accelerated filer

Accelerated filer

Non-accelerated filer (Do not check if a smaller reporting company)

Smaller reporting company

The registrant hereby amends this registration statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the registration statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

EXPLANATORY NOTE

This Post-Effective Amendment No. 1 (the "Post-Effective Amendment") relates to the Registration Statement on Form S-1 of Ignyta, Inc. (the "Company," "we," "us" or "our") pertaining to 9,010,238 shares of our common stock, \$0.00001 par value per share, which was filed with the Securities and Exchange Commission on December 19, 2013 (File No. 333-192956), as amended, and was declared effective by the Securities and Exchange Commission on February 11, 2014 (the "Registration Statement"). This Post-Effective Amendment is being filed to update certain financial and other information contained in the prospectus in accordance with Section 10(a)(3) of the Securities Act of 1933, as amended (the "Securities Act"), and includes the financials and the notes thereto included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2013 and certain other updated information contained in the Registration Statement.

No additional securities are being registered under this Post-Effective Amendment. All applicable registration fees were paid at the time of the original filing of the Registration Statement.

Table of Contents

The information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MARCH 27, 2014

PROSPECTUS

9,010,238 Shares of Common Stock

This prospectus relates to the offering and resale by the selling stockholders identified herein of up to 9,010,238 shares of common stock, par value \$0.00001 per share, of Ignyta, Inc. These shares include 7,740,142 shares of common stock issued and sold to accredited investors in a private placement offering closed on November 6, 2013, or the Initial Private Placement, and 1,270,096 shares of common stock issued and sold to accredited investors in a private placement offering closed on November 29, 2013, or the Subsequent Private Placement. We refer to the Initial Private Placement and the Subsequent Private Placement collectively as the Private Placements. All shares of common stock issued in the Private Placements were sold at a purchase price of \$6.00 per share.

The selling stockholders may sell the shares of common stock on any national securities exchange or quotation service on which the securities may be listed or quoted at the time of sale, in the over-the-counter market, in one or more transactions otherwise than on these exchanges or systems, such as privately negotiated transactions, or using a combination of these methods, and at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. See the disclosure under the heading Plan of Distribution elsewhere in this prospectus for more information about how the selling stockholders may sell or otherwise dispose of their shares of common stock hereunder.

The selling stockholders may sell any, all or none of the securities offered by this prospectus, and we do not know when or in what amount the selling stockholders may sell their shares of common stock hereunder following the effective date of this registration statement.

We will not receive any proceeds from the sale of our common stock by the selling stockholders in the offering described in this prospectus.

Our common stock is listed on the NASDAQ Capital Market under the symbol RXDX. On March 25, 2014, the last reported sale price of our common stock was \$8.95 per share.

Investing in our common stock involves a high degree of risk. Before making any investment in our common stock, you should read and carefully consider the risks described in this prospectus under Risk Factors beginning on page 8 of this prospectus.

You should rely only on the information contained in this prospectus or any prospectus supplement or amendment hereto. We have not authorized anyone to provide you with different information.

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.

This prospectus is dated , 2014

Table of Contents**TABLE OF CONTENTS**

	Page No.
<u>Prospectus Summary</u>	1
<u>Risk Factors</u>	8
<u>Special Note Regarding Forward-Looking Statements</u>	40
<u>Selling Stockholders</u>	42
<u>Plan of Distribution</u>	56
<u>Determination of Offering Price</u>	59
<u>Use of Proceeds</u>	60
<u>Description of Capital Stock</u>	61
<u>Market Price of and Dividends on our Common Stock and Related Stockholder Matters</u>	66
<u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	67
<u>Business</u>	78
<u>Management and Certain Corporate Governance Matters</u>	110
<u>Executive Compensation</u>	117
<u>Certain Relationships and Related Transactions</u>	125
<u>Security Ownership of Certain Beneficial Owners and Management</u>	127
<u>Legal Matters</u>	129
<u>Experts</u>	129
<u>Where You Can Find Additional Information</u>	129
<u>Index to Consolidated Financial Statements</u>	F-1

About This Prospectus

You should rely only on the information that we have provided or incorporated by reference in this prospectus and any applicable prospectus supplement. 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 and any applicable prospectus supplement. 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 and any applicable prospectus supplement 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 applicable prospectus supplement, 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**.

Edgar Filing: Ignyta, Inc. - Form POS AM

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.

Table of Contents

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.

Table of Contents

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.

Table of Contents

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.

Recent Developments

On March 19, 2014, we completed a public offering of 6,031,750 shares of our common stock, including the exercise in full of the underwriters' option to purchase additional shares, raising gross proceeds of approximately \$55.2 million.

The Private Placements

On November 1, 2013, we entered into a securities purchase agreement with 52 accredited investors providing for the issuance and sale to such investors of an aggregate of 7,740,142 shares of our common stock in the Initial Private Placement. The Initial Private Placement closed on November 6, 2013. The shares issued in the Initial Private Placement were sold at a purchase price per share of \$6.00, for aggregate gross proceeds to us of approximately \$46.4 million and aggregate net proceeds to us, after deducting for placement agent fees and expenses, of approximately \$44.2 million. Ladenburg Thalmann & Co. Inc. served as the placement agent in the Initial Private Placement.

On November 27, 2013, we entered into a securities purchase agreement with 195 accredited investors providing for the issuance and sale to such investors of an aggregate of 1,270,096 shares of our common stock in the Subsequent Private Placement. The Subsequent Private Placement closed on November 29, 2013. The shares issued in the Subsequent Private Placement were sold at a purchase price per share of \$6.00, for aggregate gross proceeds to us of approximately \$7.6 million and aggregate net proceeds to us, after deducting for placement agent and other offering fees and expenses, of approximately \$6.8 million. National Securities Corporation served as the placement agent in the Subsequent Private Placement.

Our aggregate gross proceeds from the Private Placements were approximately \$54.1 million, and our aggregate net proceeds from the Private Placements, after deducting for placement agent, legal, registration and other offering related fees and expenses, were approximately \$51.0 million.

The terms of the securities purchase agreements entered into with the investors in the Initial Private Placement and the Subsequent Private Placement, each of which we refer to as a Securities Purchase Agreement, contain substantially similar terms and provisions, including customary representations and warranties made by us to each of the investors and by each of the investors to us; provided, however, that the Securities Purchase Agreement we entered into in connection with the Initial Private Placement contains certain anti-dilution provisions that are not contained in the Securities Purchase Agreement we entered into in connection with the Subsequent Private Placement. Those anti-dilution provisions provide that, if we issue and sell certain of our equity securities at a purchase price per share lower than \$6.00 within the 180-day period following November 6, 2013, the investors in the Initial Private Placement shall be entitled to receive such number of additional shares of our common stock as they would have received had such lower purchase price per share been applicable in the Initial Private Placement. Certain issuances of our equity securities are not subject to those anti-dilution provisions, including: issuances pursuant to the exercise or conversion of outstanding options, warrants or other convertible securities; issuances in connection with acquisitions, asset purchases, licenses, collaborations or

Table of Contents

strategic transactions that are not for the primary purpose of raising capital; issuances to our employees, officers, directors, consultants or advisors under stock incentive plans or other arrangements that are approved by our Board of Directors; and issuances that the holders of a majority of the outstanding shares issued in the Initial Private Placement elect in writing to exclude from the application of such provisions. Both of the Securities Purchase Agreements we entered into in connection with the Initial Private Placement and the Subsequent Private Placement contain provisions that will obligate us to make certain payments to the investors thereunder if we or our transfer agent fail to timely remove certain restrictive legends from certificates representing the shares of common stock being offered hereby following the eligibility of such shares for resale under this registration statement or Rule 144 promulgated under the Securities Act of 1933, as amended, or the Securities Act.

On November 6, 2013, we entered into a registration rights agreement, or the Registration Rights Agreement, with the investors that participated in the Initial Private Placement. Upon the closing of the Subsequent Private Placement on November 29, 2013, the investors that participated in that financing became parties to and bound by, and the shares of our common stock purchased by them became subject to, the Registration Rights Agreement.

Pursuant to the terms of the Registration Rights Agreement, we agreed to file with the Securities and Exchange Commission, or the SEC, within 45 days following November 6, 2013, the registration statement of which this prospectus forms a part, to register for resale all of the 9,010,238 shares of our common stock issued in the Private Placements. As a result of our initial filing of this registration statement, we are in compliance with that filing deadline. We have also agreed to keep such registration statement effective within and for the time periods set forth in the Registration Rights Agreement. Our failure to satisfy the effectiveness requirements set forth in the Registration Rights Agreement may subject us to payment of certain monetary penalties pursuant to the terms of the Registration Rights Agreement.

Under the Registration Rights Agreement, subject to exception in certain circumstances, we have agreed to keep this registration statement effective until the later of November 6, 2014 and such time as all of the securities to be registered hereunder have been sold under this registration statement or pursuant to Rule 144 or may be sold without restriction pursuant to Rule 144. If there is not an effective registration statement covering the resale of the securities to be registered hereunder at any time during the period required by the Registration Rights Agreement, then the selling stockholders will have piggyback registration rights with respect to any such securities that are not eligible for resale pursuant to Rule 144 in connection with any other registration statement we determine to file that would permit the inclusion of those shares.

The foregoing descriptions of the Securities Purchase Agreements and the Registration Rights Agreement do not purport to be complete, and are qualified in their entirety by the complete text of those agreements, which are attached as exhibits to the registration statement of which this prospectus forms a part.

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

Table of Contents

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.

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.

Table of Contents

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.

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

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

Edgar Filing: Ignyta, Inc. - Form POS AM

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 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,

Table of Contents

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, 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.

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.

Table of Contents

The Offering

Common stock outstanding prior to this offering: 19,575,144

Common stock offered by the selling stockholders hereunder: 9,010,238

Common stock to be outstanding after this offering: 19,575,144

Use of Proceeds: We will not receive any proceeds from the sale of our common stock offered by the selling stockholders under this prospectus.

Risk Factors: Investing in our securities involves a high degree of risk and purchasers may lose their entire investment. See the disclosure under the heading Risk Factors beginning on page 8 of this prospectus.

NASDAQ Capital Market Symbol: RXDX

The number of shares of our common stock outstanding prior to and after this offering is based on 19,575,144 shares of common stock outstanding as of March 25, 2014, and excludes:

1,643,488 shares of common stock issuable upon the exercise of outstanding stock options as of March 25, 2014, at a weighted average exercise price of \$5.94 per share;

41,668 shares of common stock issuable upon the exercise of outstanding warrants as of March 25, 2014, at a weighted average exercise price of \$4.20 per share; and

1,048,356 shares of common stock reserved for future issuance under our Amended and Restated 2011 Stock Incentive Plan, or the Ignyta Plan, as of March 25, 2014.

Table of Contents

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 and the loan from SVB, 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 development of RXDX-101 and

Table of Contents

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, we issued an aggregate of 9,010,238 shares of our common stock. 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;

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

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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;

Table of Contents

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.

Table of Contents

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;

Table of Contents

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.

Table of Contents

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

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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

Table of Contents

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

Table of Contents

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

Table of Contents

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.

Table of Contents

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.

Table of Contents

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;

Table of Contents

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

Table of Contents

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, the Private Placements and/or our March 2014 public offering, and may experience one or more ownership changes as a result of 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 we experience any 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.

Table of Contents

Risks Related to Ownership of our Common Stock

There may not be a viable public market for our common stock and as a result it may be difficult for you to sell your shares of our common stock.

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

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

The 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;

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;

Table of Contents

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.

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. As of March 25, 2014, a total of 19,575,144 shares of our common stock were outstanding. We issued 6,031,750 shares of our common stock in a public offering that closed on March 19, 2014, which shares are registered under the Securities Act and are freely tradable without restriction. Upon the effectiveness of the registration statement of which this prospectus forms a part, 15,049,324 shares of our common stock will be registered under the Securities Act and will be freely tradable without restriction. Any sales of those shares or any perception in the market that such sales may occur could cause the trading price of our common stock to decline. Additionally, the 4,516,469 outstanding shares of our common stock that we issued to former stockholders of Ignyta Operating in connection with the closing of the merger in which Ignyta Operating became our wholly owned subsidiary will become freely tradable upon the expiration of certain lock-up restrictions applicable to those shares, which prohibit their sale, disposition or other transfer for a period of 180 days following the closing of the Initial Private Placement, and the lapse of securities law restrictions on their resale, which could occur under Rule 144 after the end of the 12-month period following November 1, 2013, the date on which we initially filed with the SEC our Current Report on Form 8-K containing Form 10 information.

Table of Contents

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

the selling stockholders named in such registration statement may continue to offer shares covered by the resale registration statement for a significant period of time, the precise duration of which cannot be predicted. Accordingly, the adverse market and price pressures resulting from an offering pursuant to the resale registration statement may continue for an extended period of time and continued negative pressure on the market price of our common stock could have a material adverse effect on our ability to raise additional equity capital.

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

The trading market for our common stock depends in part on the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on us or our business. If no securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively affected. If securities or industry analysts initiate coverage, and one or more of those analysts downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price would likely decline. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our stock could decrease, which might cause our stock price and trading volume to decline.

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

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

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

We may be exposed to additional risks because the business of Ignyta Operating has become a public company through a reverse merger transaction. There has been increased focus in recent years by government agencies on transactions such as the merger in which Ignyta Operating became our wholly owned subsidiary, and we may be subject to increased scrutiny by the SEC and other government agencies and holders of our securities as a result of the completion of that transaction. Further, as a result of our existence as a shell company under applicable rules of the SEC prior to the closing of the merger on October 31, 2013, we are subject to certain restrictions and limitations for certain specified periods of time relating to potential future issuances of our securities and compliance with applicable SEC rules and regulations. Additionally, our going public by means of a reverse merger transaction may make it more

difficult for us to obtain coverage from securities analysts of

Table of Contents

major brokerage firms following the merger because there may be little incentive to those brokerage firms to recommend the purchase of our common stock. The occurrence of any such event could cause our business or stock price to suffer.

We will incur increased costs associated with, and our management will need to devote substantial time and effort to, compliance with public company reporting and other requirements.

As a public company listed on the NASDAQ Capital Market, and particularly if and after we cease to be an emerging growth company or a smaller reporting company, we will incur significant legal, accounting and other expenses that we did not incur prior to the listing of our common stock on the NASDAQ Capital Market. In addition, the rules and regulations of the SEC and the NASDAQ Capital Market impose numerous requirements on public companies, including requirements relating to our corporate governance practices, with which we will need to comply. Further, since we are subject to the Exchange Act, we are required to, among other things, file annual, quarterly and current reports with respect to our business and operating results. Our management and other personnel will need to devote substantial time to gaining expertise regarding operations as a public company and compliance with applicable laws and regulations, and our efforts and initiatives to comply with those requirements could be expensive.

Ignyta Operating was not subject to requirements to establish, and did not establish, internal control over financial reporting and disclosure controls and procedures prior to the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary. Our management team and Board of Directors will need to devote significant efforts to maintaining adequate and effective disclosure controls and procedures and internal control over financial reporting in order to comply with applicable regulations, which may include hiring additional legal, financial reporting and other finance and accounting staff and engaging consultants to assist in designing and implementing such procedures. Additionally, any of our efforts to improve our internal controls and design, implement and maintain an adequate system of disclosure controls may not be successful and will require that we expend significant cash and other resources.

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

We are required to comply with certain aspects of Section 404 of the Sarbanes-Oxley Act of 2002. Section 404 of the Sarbanes-Oxley Act requires public companies to, among other things, conduct an annual review and evaluation of their internal controls. Ensuring that we have adequate internal financial and accounting controls and procedures in place so that we can produce accurate financial statements on a timely basis is a costly and time-consuming effort that will need to be evaluated frequently. Our failure to maintain the effectiveness of our internal controls in accordance with the requirements of the Sarbanes-Oxley Act could have a material adverse effect on our business. We could lose investor confidence in the accuracy and completeness of our financial reports, which could have an adverse effect on the price of our common stock. In addition, if our efforts to comply with new or changed laws, regulations and standards differ from the activities intended by regulatory or governing bodies due to ambiguities related to practice, regulatory authorities may initiate legal proceedings against us and our business may be harmed.

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

We are an emerging growth company under the JOBS Act. We are also a smaller reporting company as defined in applicable rules under the Exchange Act. As an emerging growth company and a smaller reporting

Table of Contents

company, we are eligible to take advantage of certain extended accounting standards and exemptions from various reporting requirements that are not available to public reporting companies that do not qualify for those classifications. For instance, we are exempt from any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and financial statements, commonly known as an auditor discussion and analysis; we are not required to hold a nonbinding advisory stockholder vote on executive compensation or any golden parachute payments not previously approved by stockholders; we are not required to comply with the requirement of auditor attestation of management's assessment of internal control over financial reporting, which is required for some other public reporting companies by Section 404 of the Sarbanes-Oxley Act of 2002; we are eligible for reduced disclosure obligations regarding executive compensation in our periodic and annual reports; and we are eligible for reduced financial statement disclosure in any registration statements under the Securities Act or reports under the Exchange Act that we may file. For as long as we continue to be an emerging growth company and/or a smaller reporting company, which we anticipate will be for the foreseeable future, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of those respective classifications. As a result, our publicly available disclosure may not be as robust or comprehensive as that of other public reporting companies that do not qualify for those classifications.

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

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

Certain of our executive officers, directors and large stockholders own a significant percentage of our outstanding capital stock. As of February 28, 2014, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 32% of our outstanding voting stock (which includes shares they had the right to acquire within 60 days). Accordingly, our directors and executive officers and large stockholders have significant influence over our affairs due to their substantial ownership coupled with the positions of some of these stockholders on our management team, and have substantial voting power to approve matters requiring the approval of our stockholders. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets or other major corporate transaction. This concentration of ownership in our Board of Directors and management team and certain other large stockholders may prevent or discourage unsolicited acquisition proposals or offers for our common stock that some of our stockholders may believe is in their best interest.

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

Our Amended and Restated Articles of Incorporation authorize the issuance of up to 100,000,000 shares of our common stock and up to 10,000,000 shares of preferred stock with the rights, preferences and privileges that our Board of Directors may determine from time to time. Upon the closing of the Private Placements, we issued an aggregate of 9,010,238 shares of our common stock. On March 19, 2014, we issued 6,031,750 shares of our common stock upon the closing of a public offering. In addition to capital raising activities such as public and private placements of our common stock, which we expect to continue to pursue in order to raise the funding we will need in order to continue our operations, other possible business and financial uses for our authorized capital stock include,

without limitation, future stock splits, acquiring other companies, businesses or products in exchange for shares of our capital stock, issuing shares of our capital stock to partners or other collaborators in

Table of Contents

connection with strategic alliances, attracting and retaining employees by the issuance of additional securities under our equity compensation plans, or other transactions and corporate purposes that our Board of Directors deems are in the best interest of our company. Additionally, shares of our capital stock could be used for anti-takeover purposes or to delay or prevent changes in control or our management. Any future issuances of shares of our capital stock may not be made on favorable terms or at all, they may not enhance stockholder value, they may have rights, preferences and privileges that are superior to those of our common stock, and they may have an adverse effect on our business or the trading price of our common stock. The issuance of any additional shares of our common stock will reduce the book value per share and may contribute to a reduction in the market price of the outstanding shares of our common stock. Additionally, any such issuance will reduce the proportionate ownership and voting power of all of our current stockholders.

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

Even after giving effect to the funds raised in the Private Placements, we expect that significant additional capital will be needed in the future to continue our planned operations. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors in a prior transaction may be materially diluted. Additionally, new investors could gain rights, preferences and privileges senior to those of existing holders of our common stock. Further, any future sales of our common stock by us or resales of our common stock by our existing stockholders could cause the market price of our common stock to decline.

Pursuant to our Amended and Restated 2011 Stock Incentive Plan, or the Ignyta Plan, we are authorized to grant equity awards to our employees, directors and consultants for up to an aggregate of 2,712,652 shares of our common stock. Additionally, as of February 28, 2014, there were outstanding options granted under the Ignyta Plan that are exercisable for up to 1,675,153 shares of our common stock, and there were outstanding warrants to acquire up to 41,668 shares of our common stock. Any future grants of options, warrants or other securities exercisable or convertible into our common stock, or the exercise or conversion of such shares, and any sales of such shares in the market, could have an adverse effect on the market price of our common stock.

Some provisions of our charter documents and Nevada law may discourage an acquisition of us by others, even if the acquisition may be beneficial to some of our stockholders.

Provisions in our Amended and Restated Articles of Incorporation and Bylaws, as well as certain provisions of Nevada law, could make it more difficult for a third-party to acquire us, even if doing so may benefit some of our stockholders. These provisions include the authorization of 10,000,000 shares of blank check preferred stock, the rights, preferences and privileges of which may be established and shares of which may be issued by our Board of Directors at its discretion from time to time and without stockholder approval.

Because we are incorporated in Nevada, we may in the future be governed by Nevada's statutes governing combinations with interested stockholders and control share acquisitions, which may discourage, delay or prevent someone from acquiring us or merging with us, whether or not it is desired by or beneficial to our stockholders. However, we are not at this time subject to Nevada's laws governing combinations with interested stockholders because we have elected to opt out of such laws in our Amended and Restated Articles of Incorporation, and we believe that we are not at this time subject to Nevada's control share acquisition laws because they apply only to Nevada corporations with at least 100 Nevada residents as stockholders of record.

Any provision of our Amended and Restated Articles of Incorporation or Bylaws or of Nevada law that is currently or in the future applicable to us and has the effect of delaying or deterring a change in control could

Table of Contents

limit the opportunity for our stockholders to receive a premium for their shares of our common stock in the event that a potentially beneficial acquisition is discouraged, and could also affect the price that some investors are willing to pay for our common stock.

The elimination of personal liability against our directors and officers under Nevada law and the existence of indemnification rights held by our directors, officers and employees may result in substantial expenses.

Our Amended and Restated Articles of Incorporation and our Bylaws eliminate the personal liability of our directors and officers to us and our stockholders for damages for breach of fiduciary duty as a director or officer to the extent permissible under Nevada law. Further, our Amended and Restated Articles of Incorporation and our Bylaws and individual indemnification agreements we have entered with each of our directors and executive officers provide that we are obligated to indemnify each of our directors or officers to the fullest extent authorized by the Nevada law and, subject to certain conditions, advance the expenses incurred by any director or officer in defending any action, suit or proceeding prior to its final disposition. Those indemnification obligations could expose us to substantial expenditures to cover the cost of settlement or damage awards against our directors or officers, which we may be unable to afford. Further, those provisions and resulting costs may discourage us or our stockholders from bringing a lawsuit against any of our current or former directors or officers for breaches of their fiduciary duties, even if such actions might otherwise benefit our stockholders.

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

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

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements in this prospectus that are not descriptions of historical facts, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated products, are forward-looking statements that are based on management's current expectations and assumptions and are subject to risks and uncertainties. If such risks or uncertainties materialize or such assumptions prove incorrect, our business, operating results, financial condition and stock price could be materially negatively affected. In some cases, you can identify forward-looking statements by terminology including anticipates, believes, can, continue, could, estimates, expects, intends, may, plans, potential, would or the negative of these terms or other comparable terminology. Factors that could cause actual results to differ materially from those currently anticipated include those set forth in the section titled Risk Factors including, without limitation, risks relating to:

the results of our research and development activities, including uncertainties relating to the discovery of potential product candidates and the preclinical and clinical testing of our product candidates;

the early stage of our product candidates presently under development;

our ability to obtain and, if obtained, maintain regulatory approval of our current product candidates, and any of our other future product candidates, and any related restrictions, limitations and/or warnings in the label of any approved product candidate;

our need for substantial additional funds in order to pursue our business plan and the uncertainty of whether we will be able to obtain the funding we need;

our ability to retain or hire key scientific or management personnel;

our ability, with partners, to validate, develop and obtain regulatory approval of companion diagnostics for our product candidates;

our ability to protect our intellectual property rights, including patent and other intellectual property rights;

our dependence on third-party manufacturers, suppliers, research organizations, testing laboratories and other potential collaborators;

our ability to develop successful sales and marketing capabilities in the future as needed;

the size and growth of the potential markets for any of our product candidates, and the rate and degree of market acceptance of any of our product candidates;

competition in our industry;

the impact of healthcare reform legislation; and

regulatory developments in the United States and foreign countries.

We operate in a very competitive and rapidly-changing environment and new risks emerge from time to time. As a result, it is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to

Table of Contents

differ materially from those contained in any forward-looking statements we may make. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this prospectus may not occur and actual results could differ materially and adversely from those anticipated or implied in the forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee that the future results, levels of activity, performance or events and circumstances reflected in the forward-looking statements will be achieved or occur. Moreover, neither we nor any other person assumes responsibility for the accuracy and completeness of the forward-looking statements. The forward-looking statements included in this prospectus speak only as of the date hereof, and except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus to conform these statements to actual results or to changes in our expectations. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Table of Contents

SELLING STOCKHOLDERS

This prospectus covers the resale from time to time by the selling stockholders identified in the table below of up to an aggregate of 9,010,238 issued and outstanding shares of our common stock issued and sold to investors in the Private Placements, 7,740,142 of which were issued and sold to investors in the Initial Private Placement and 1,270,096 of which were issued and sold to investors in the Subsequent Private Placement.

Pursuant to the Registration Rights Agreement, we have filed with the SEC the registration statement of which this prospectus forms a part in order to register such resales of our common stock under the Securities Act. We have also agreed to cause this registration statement to become effective and to keep such registration statement effective within and for the time periods set forth in the Registration Rights Agreement. Our failure to satisfy the filing or effectiveness deadlines set forth in the Registration Rights Agreement may subject us to payment of certain monetary penalties pursuant to the terms of the Registration Rights Agreement.

The selling stockholders identified in the table below may from time to time offer and sell under this prospectus any or all of the shares of common stock described under the column Shares of Common Stock Being Offered in this Offering in the table below. The table below has been prepared based upon information furnished to us by the selling stockholders as of the dates represented in the footnotes accompanying the table. The selling stockholders identified below may have sold, transferred or otherwise disposed of some or all of their shares since the date on which the information in the following table is presented in transactions exempt from or not subject to the registration requirements of the Securities Act. Information concerning the selling stockholders may change from time to time and, if necessary, we will amend or supplement this prospectus accordingly and as required.

We have been advised, as noted in the footnotes in the table below, that none of the selling stockholders is a broker-dealer and that certain of the selling stockholders are affiliates of a broker-dealer and/or underwriter. Those selling stockholders have informed us that they bought our securities in the ordinary course of business, and that none of these selling stockholders had, at the time of their purchase of our securities, any agreements or understandings, directly or indirectly, with any person to distribute such securities.

The following table and footnote disclosure following the table sets forth the name of each selling stockholder, the nature of any position, office or other material relationship, if any, that the selling stockholder has had within the past three years with us or with any of our predecessors or affiliates, and the number of shares of our common stock beneficially owned by the selling stockholder before this offering. The number of shares reflected are those beneficially owned, as determined under applicable rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under applicable SEC rules, beneficial ownership includes any shares of common stock as to which a person has sole or shared voting power or investment power and any shares of common stock which the person has the right to acquire within 60 days after the date as of which such number is given, through the exercise of any option, warrant or right or through the conversion of any convertible security. Unless otherwise indicated in the footnotes to the table below and subject to community property laws where applicable, we believe, based on information furnished to us, that each of the selling stockholders named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned.

We have assumed that all shares of common stock reflected in the table as being offered in the offering covered by this prospectus will be sold from time to time in this offering. We cannot provide an estimate as to the number of shares of common stock that will be held by the selling stockholders upon termination of the offering covered by this prospectus because the selling stockholders may offer some, all or none of their shares of common stock being offered in the offering.

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Shares of Common Stock Beneficially Owned Before this Offering	Percentage of Outstanding Common Stock Beneficially Owned Before this Offering (1)	Shares of Common Stock Being Offered in this Offering	Shares of Common Stock Beneficially Owned Upon Completion of this Offering (2)	Percentage of Outstanding Common Stock Beneficially Owned Upon Completion of this Offering (1)(2)
<i>Investors in the Initial Private Placement (3)</i>							
1798 Fundamental Strategies							
Master Fund Ltd.	§	(4)	665,000	3.40%	665,000		
2B LLC		(5)	83,333	*	83,333		
667, L.P. (Account #1)		(6)	39,167	*	39,167		
667, L.P. (Account #2)		(6)	27,572	*	27,572		
Alan G. Hassenfeld 1998							
Revocable Trust Dtd 4/28/98		(7)	41,700	*	41,700		
Arbco Partners, LP		(8)	16,667	*	16,667		
Armistice Capital Master Fund							
Ltd.		(9)	500,000	2.55%	500,000		
Baker Brothers Life Sciences, L.P.							
		(6)	516,561	2.64%	516,561		
BioBrit, LLC		(10)	133,333	*	33,333	100,000	*
Boxer Capital, LLC		(11)	544,667	2.78%	544,667		
Broadfin Healthcare Master							
Fund, LTD		(12)	416,700	2.13%	416,700		
Bryan Paul Horton 1998							
Grantors Trust		(13)	16,667	*	16,667		
Capital Ventures International	§	(14)	41,600	*	41,600		
Alexander Casdin		(15)	105,369	*	50,000	55,369	*
Casdin Partners Master Fund, LP		(16)	50,000	*	50,000		
Eric Caslow		(17)	83,334	*	16,667	66,667	*
City Hill Venture Partners I, LLC							
		(18)	3,316,668	16.94%	333,334	2,983,334	15.24%
DAFNA Lifescience LTD							
		(19)	27,000	*	27,000		
DAFNA Lifescience Market							
Neutral LTD		(19)	5,700	*	5,700		
DAFNA Lifescience Select LTD		(19)	50,700	*	50,700		
Del Mar Master Fund, Ltd.		(20)	166,666	*	166,666		
Dinver, LLC		(21)	91,667	*	25,000	66,667	*
Empery Asset Master, Ltd		(22)	41,600	*	41,600		
Foresite Capital Fund I, L.P.		(23)	500,000	2.55%	500,000		
Fourth Avenue Capital Partners							
LP		(24)	171,667	*	171,667		

Edgar Filing: Ignyta, Inc. - Form POS AM

Colby Harlow	(25)	16,667	*	16,667
HFR HE Sphera Global Healthcare Master Trust	(26)	12,034	*	12,034
Independence Capital Select Health Care Fund, L.P.	(27)	8,400	*	8,400
Kevin A. Wechter Irrevocable Trust	(28)	16,667	*	16,667
KKH Family Limited Partnership	(29)	16,667	*	16,667
Devraj Lahiri		8,340	*	8,340
LSM Capital Inc.	(30)	85,000	*	85,000
Thomas Malley		41,600	*	41,600
Andrew McDonald	§ (31)	83,333	*	83,333

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Shares of Common Stock Beneficially Owned Before this Offering	Percentage of Outstanding Common Stock Beneficially Owned Before this Offering (1)	Shares of Common Stock Being Offered in this Offering	Percentage of Outstanding Common Stock Beneficially Owned Upon Completion of this Offering (2)	Percentage of Outstanding Common Stock Beneficially Owned Upon Completion of this Offering (1)(2)
Merlin Nexus IV, LP		(32)	400,000	2.04%	400,000		
Monashee Investment Management LLC		(33)	100,000	*	100,000		
MVA Investors, LLC		(34)	83,333	*	83,333		
David Odmark			30,000	*	30,000		
Pacific Equity Ventures, L.P.		(35)	16,667	*	16,667		
Harkishan B. Parekh			29,167	*	29,167		
R. Finkelstein Inherited IRA Beneficiary of Milton Finkelstein		(36)	20,000	*	20,000		
Christopher Reyes			8,333	*	8,333		
Yehuda M. Rice	§	(31)	83,333	*	83,333		
Robert A. Fink & Jessica K. Fink Family Trust		(37)	16,667	*	16,667		
Abhijit Roy			15,000	*	15,000		
Sabby Healthcare Volatility Master Fund, Ltd.		(38)	550,000	2.81%	550,000		
Jay B. Silverman			16,667	*	16,667		
Sphera Global Healthcare Master Fund		(26)	192,966	*	192,966		
David J. Strupp, Jr.	§	(39)	8,333	*	8,333		
Three Arch Opportunity Fund LP		(5)	249,667	1.28%	249,667		
venBio Select Fund LLC		(40)	416,700	2.13%	416,700		
Visium Balanced Master Fund, Ltd.		(41)	833,300	4.26%	833,300		
<i>Investors in the Subsequent Private Placement (42)</i>							
3MD Partnership, Ltd.		(43)	4,100	*	4,100		
Carlo Alberici			3,000	*	3,000		
Andrew Alltizer			4,000	*	4,000		
Ann Robbins Cohen Trust		(44)	4,000	*	4,000		
Todd G. Bari			3,000	*	3,000		
Kevin Barry			5,000	*	5,000		
John R. Bartos			10,000	*	10,000		
Peter C. Beale			3,500	*	3,500		
Anthony Behette			10,000	*	10,000		

Edgar Filing: Ignyta, Inc. - Form POS AM

Madeleine Behette		10,000	*	10,000
Marguerite Behette-Hart		10,000	*	10,000
George E. Berkey		3,000	*	3,000
Robert Biederman		4,000	*	4,000
Blue Ocean LLC	§ (45)	10,000	*	10,000
Douglas Brody		3,000	*	3,000
David C. Bukzin		7,000	*	7,000
Jeffrey J. Bunker		3,000	*	3,000

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Percentage of Outstanding		Percentage of Shares of Outstanding Common Stock	
			Shares of Common Stock Beneficially Owned Before this Offering	Common Stock Beneficially Owned Before this Offering (1)	Shares of Common Stock Offered in this Offering	Beneficially Owned Upon Completion of this Offering (2)
Salvatore Thomas and Jacqueline Butera, JT WROS			3,000	*	3,000	
Allen and Jolaine Cage, JT WROS			5,000	*	5,000	
John Brad Carlin			3,000	*	3,000	
Gary W. Carlisle			4,000	*	4,000	
Chary Corp.		(46)	6,000	*	6,000	
Wilson Chen			5,000	*	5,000	
Eugene and Jennifer Chen, JT WROS			10,000	*	10,000	
Craig Child			4,300	*	4,300	
Jack Chitayat			16,666	*	16,666	
Choe Ramsay Family Trust		(47)	93,334	*	10,000	83,334 *
Lawrence Coolidge			10,000	*	10,000	
Nancy Myers Coolidge			10,000	*	10,000	
Ray Crespo			10,000	*	10,000	
John E. Crisp			10,000	*	10,000	
Michael Cullen			7,000	*	7,000	
Mario Dell Aera			4,000	*	4,000	
Jules DeVigne			10,000	*	10,000	
Jules and Deborah G. DeVigne, JT WROS			10,000	*	10,000	
Joseph M. Diangelo			4,166	*	4,166	
DJDDT Properties, LLC	§	(45)	10,000	*	10,000	
Charles Dossett			10,000	*	10,000	
Dr. David Shively Rev Dynastic With Preservation Trust		(48)	8,300	*	8,300	
East Hudson Enterprise, Inc.		(49)	4,000	*	4,000	
Michael Ebedes			3,000	*	3,000	
Environeering, Inc.		(50)	3,000	*	3,000	
Albert B. Erwin Jr.			4,000	*	4,000	
Jason Fadeyi		(51)	10,000	*	10,000	
Jarter L. Fang			5,000	*	5,000	
Brett Ferenchak			4,000	*	4,000	
Craig D. and Lisa E. Fishman, JT WROS			10,000	*	10,000	
James W. Flynn			3,000	*	3,000	

Edgar Filing: Ignyta, Inc. - Form POS AM

Barry Frost		3,000	*	3,000
Howard K. Fuguet		3,000	*	3,000
G. O Connor Trust	(52)	10,000	*	10,000
Kevin Gabrik		5,000	*	5,000
Thomas and Suzan Mary Garrity, JT				
WROS		3,000	*	3,000

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Percentage of Outstanding		Percentage of Outstanding	
			Shares of Common Stock Beneficially Owned Before this Offering	Percentage of Common Stock Beneficially Owned Before this Offering (1)	Shares of Common Stock Being Offered in this Offering	Percentage of Common Stock Beneficially Owned Upon Completion of this Offering (2)
Larry Gelbfish			3,000	*	3,000	
Thomas V. Gerardi			6,666	*	6,666	
Michael P. Giannelli			10,000	*	10,000	
Tom Giftos			3,000	*	3,000	
Karen Jean and Raymond Gary Gilmore, JT WROS		(53)	3,000	*	3,000	
Glendenning Investment Group		(54)	4,000	*	4,000	
David Mark Goldhagen			5,000	*	5,000	
Jonathan Gralnick			3,000	*	3,000	
Douglas Grant		(55)	10,000	*	10,000	
Grant's Engineering and Machine Company		(56)	8,000	*	8,000	
GST Exempt Trust Created Under Jacob Lomazow Rev. Trust		(57)	5,000	*	5,000	
Ellis R. Guilbeau			3,000	*	3,000	
Jack Guiragosian			3,000	*	3,000	
Gunther Well and Pump Services, LLC		(58)	6,000	*	6,000	
Michael Hafke			10,000	*	10,000	
Terry G. Han			5,000	*	5,000	
Dr. Larry Hauskins			5,000	*	5,000	
Tom Herburger			6,000	*	6,000	
Alan Hertz			4,500	*	4,500	
Julie and Michael Hess, JT WROS			10,000	*	10,000	
Dr. Kevin Hsu			5,000	*	5,000	
William Huff			8,300	*	8,300	
Gregory Hurley			10,000	*	10,000	
Grady S. Hurley			3,000	*	3,000	
David W. English			10,000	*	10,000	
Keith Jackson			4,000	*	4,000	
David Jarrett			5,000	*	5,000	
Jastco Mayfair Intl. Property, LLC		(59)	10,000	*	10,000	
Richard Johnson			3,000	*	3,000	
John G. Kalyvas			4,000	*	4,000	
Robert Kaufman			83,333	*	83,333	
Alon Kessler			3,000	*	3,000	

Edgar Filing: Ignyta, Inc. - Form POS AM

Stefan and Kerstin Kneis, JT WROS	8,500	*	8,500
William M. and Joy S. Kong, JT WROS	3,500	*	3,500
Michael Kontos	7,916	*	7,916
Steve Kontos	7,916	*	7,916
Michael D. Langan	3,000	*	3,000

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Percentage of Outstanding Common Stock		Percentage of Shares of Outstanding Common Stock	
			Shares of Common Stock Beneficially Owned Before this Offering	Common Stock Beneficially Owned Before this Offering (1)	Shares of Common Stock Offered in this Offering	Beneficially Owned Upon Completion of this Offering (2)
Kenneth Laviano			3,000	*	3,000	
Patrick T. Lee			10,000	*	10,000	
Ruby B. Lee			15,000	*	15,000	
Moe H. Leichter			5,000	*	5,000	
Edward Lopez			4,500	*	4,500	
John Charles Lewis and Susan Elizabeth Kenney, JT WROS			3,000	*	3,000	
William L. and Rita M. Lurie, JT WROS			5,000	*	5,000	
Terry and Cindy Sue Mace, JT WROS			13,000	*	13,000	
John Maddux		(60)	5,000	*	5,000	
Luigi Mancini			3,000	*	3,000	
George R. Martin			4,000	*	4,000	
Tanvir Ali Master			5,000	*	5,000	
Duane H. Mathiowetz			10,000	*	10,000	
Carol H. Price and Duane Mathiowetz, JT WROS			10,000	*	10,000	
Tony Y. Maung		(61)	43,334	*	10,000	33,334 *
Max G. Johnson TTEE/Max Johnson Living Trust U/A 1-7-99		(62)	10,000	*	10,000	
James P. McCarthy			10,000	*	10,000	
John S. and Linda M. McPhee, JT WROS			10,000	*	10,000	
Marvin Mermelstein			3,000	*	3,000	
Duncan J. Milcetic			4,000	*	4,000	
Stanley B. Miles			3,500	*	3,500	
Jeffrey Miller			4,000	*	4,000	
Jan P. Miller			4,000	*	4,000	
Mehrdad Mark and Mona Zohdi Mofid, JT WROS			10,000	*	10,000	
Jorge Morazzani			3,000	*	3,000	
Timothy Moreau			6,000	*	6,000	
Michael A. Mullen		(63)	3,000	*	3,000	
Simon and Enas Muzio, JT WROS			3,000	*	3,000	
Navy Bancorp, Inc.		(64)	3,000	*	3,000	

Edgar Filing: Ignyta, Inc. - Form POS AM

Harry Neff	5,000	*	5,000
Roger Nesbitt	5,000	*	5,000
Keith O. Newton	4,167	*	4,167
NFS/FMTC IRA FBO Paul D. McKinney	10,000	*	10,000

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Percentage	Percentage	Percentage
			of Outstanding Shares of Common Stock Beneficially Owned Before this Offering (1)	of Outstanding Shares of Common Stock Beneficially Owned Before this Offering (1)	of Outstanding Common Stock Beneficially Owned Upon Completion of this Offering (2)
NFS/FMTC IRA FBO Stanley Michael Rein			3,000	*	3,000
NFS/FMTC IRRL FBO Brian A. Anderson			3,000	*	3,000
NFS/FMTC Rollover IRA FBO Daniel Wickard			4,000	*	4,000
NFS/FMTC Rollover IRA FBO Gary Schulz			5,000	*	5,000
NFS/FMTC Rollover IRA FBO Jim Brummer			4,000	*	4,000
NFS/FMTC Rollover IRA FBO Michael Accardi			4,000	*	4,000
NFS/FMTC Rollover IRA FBO Timothy W. Hansen			8,333	*	8,333
NFS/FMTC SEP IRA FBO Terry Mace			3,000	*	3,000
NFS/FMTC SEP IRA FBO William Miller			5,000	*	5,000
NFS/FMTC Simple IRA Robertson Electric Co; Inc. FBO Bruce Locker			5,000	*	5,000
NFS/FMTC Traditional IRA FBO Normand F. Smith			10,000	*	10,000
NFS/FMTC Traditional IRA FBO Robert Gordon			4,000	*	4,000
NFS/FMTC Traditional IRA FBO Roger Nesbitt			5,000	*	5,000
NFS/FMTC Traditional IRA FBO Steven Vuyovich			7,000	*	7,000
Russell Nowak			9,000	*	9,000
Stefan Nowina			10,000	*	10,000
Tanju and Tina Obut, JT WROS			8,000	*	8,000
David B. O'Neill			4,000	*	4,000
Michael Padgett			4,000	*	4,000
Paramount Biosciences, LLC	§	(45)	10,000	*	10,000
Sharad and Chandrikda Patel, JT WROS			3,000	*	3,000

Edgar Filing: Ignyta, Inc. - Form POS AM

Timothy E. Pauling		4,000	*	4,000
Lowell Pearson		3,000	*	3,000
Randy Perillo		10,000	*	10,000
PJS, Inc.	(65)	5,000	*	5,000
Tony G. Puckett		3,000	*	3,000

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Percentage of Outstanding		Percentage of Outstanding	
			Shares of Common Stock Beneficially Owned Before this Offering	Percentage of Common Stock Beneficially Owned Before this Offering (1)	Shares of Common Stock Being Offered in this Offering	Percentage of Common Stock Beneficially Owned Upon Completion of this Offering (2)
Bobby Purcell			3,000	*	3,000	
RAQ LLC	§	(45)	10,000	*	10,000	
James G. Reed			8,333	*	8,333	
Reesman s Excavating and Grading, Inc.		(66)	10,000	*	10,000	
Rhoda Ann Miller Trust		(67)	10,000	*	10,000	
William Ristvedt			3,000	*	3,000	
RNW LLC	§	(45)	10,000	*	10,000	
Lindsay A. Rosenwald, M.D.	§	(68)	10,000	*	10,000	
Patrick C. Sargent			10,000	*	10,000	
Daniel N. and Elizabeth Sauder, JY WROS			10,000	*	10,000	
Earl Sauls			4,000	*	4,000	
Lloyd and Deborah Schill, JT WROS			3,500	*	3,500	
David and Carolyn Schmitz, JT WROS			4,000	*	4,000	
John and Rosemary E. Schneider, JT WROS			3,000	*	3,000	
Mark Schordock			3,000	*	3,000	
Roger J. Schwarz			10,000	*	10,000	
Donald P. Sesterhenn			4,000	*	4,000	
Dr. David Shively		(69)	8,300	*	8,300	
Stuart Simpson			3,000	*	3,000	
Navin Singh			10,000	*	10,000	
Brian Skillern			4,300	*	4,300	
Joseph P. Slattery			4,000	*	4,000	
James Somers			5,000	*	5,000	
Sooner Ranch Investments, LP		(70)	3,000	*	3,000	
Yaroslav Stakhiv			4,000	*	4,000	
Pasquale V. and Maria Stiso, JT WROS			3,000	*	3,000	
Jeffrey J. Stoen			4,000	*	4,000	
Gary L. Sturm			10,000	*	10,000	
Patrick Raymond Sullivan			10,000	*	10,000	
Scott L. Summers			3,000	*	3,000	
Norman Sunamoto			10,000	*	10,000	

Edgar Filing: Ignyta, Inc. - Form POS AM

Sunstone Partners, LLC	(71)	9,000	*	9,000
Tech Plan Inc.	(72)	10,000	*	10,000
The Ginsburg Family Trust	(73)	2,000	*	2,000
Thomas C. Tillotson		3,000	*	3,000
Tony L. Chang and Tinyee T. Chang Rev. Trust 2013 DTD 10/28/13	(74)	10,000	*	10,000

Table of Contents

Selling Stockholder	Broker-dealer Affiliate	Footnote, if any	Percentage of Outstanding		Percentage of Outstanding	
			Shares of Common Stock Beneficially Owned Before this Offering	Percentage of Common Stock Beneficially Owned Before this Offering (1)	Shares of Common Stock Being Offered in this Offering	Percentage of Common Stock Beneficially Owned Upon Completion of this Offering (2)
Robert C. Towns			3,000	*	3,000	(1)(2)
Tsai Family Trust		(75)	5,000	*	5,000	
Daniel T. and Lilliam T. Tsai, JT WROS			5,000	*	5,000	
Stanley O. Uptigrove			3,500	*	3,500	
Nick Valk			5,000	*	5,000	
Steven J. and Mary E. Vuyovich, JT WROS			3,000	*	3,000	
Rush M. Waite			10,000	*	10,000	
R.B. Wilchar			5,000	*	5,000	
Wing Real Estate, LLC		(76)	10,000	*	10,000	
Steve and Patricia Wubker, JT WROS			10,000	*	10,000	

* Less than 1%.

§ The selling stockholder is an affiliate of a broker-dealer.

- (1) Percentage ownership is based on a denominator equal to the sum of (i) 19,575,144 shares of our common stock outstanding as of March 25, 2014, and (ii) the number of shares of common stock issuable upon exercise or conversion of convertible securities beneficially owned by the applicable selling stockholder.
- (2) Assumes that all shares of common stock being registered under the registration statement of which this prospectus forms a part are sold in this offering, and that none of the selling stockholders acquire additional shares of our common stock after the date of this prospectus and prior to completion of this offering.
- (3) All information regarding investors in the Initial Private Placement is provided as of November 6, 2013.
- (4) Lombard Odier Asset Management (USA) Corp. is the investment adviser to the selling stockholder and as such it and its portfolio manager Allan Reine have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities. Mr. Reine disclaims beneficial ownership of such securities, except to the extent of his pecuniary interest therein.
- (5) Longwood Capital Partners LLC is the investment advisor and general partner to the selling stockholder and as such it and its managing member Richard Lin have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (6) The selling stockholder is under the advisement of Baker Brothers Advisors LP and as such is, and Julian C. Baker and Felix J. Baker, have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (7) Alan G. Hassenfeld, the trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.

- (8) Colby Harlow, the managing partner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (9) Steven Boyd, the owner of Armistice Capital LLC which controls the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (10) Includes the following securities that are not being offered in this offering: 100,000 shares of our common stock held of record by the selling stockholder. Daniel Mark Bradbury, the managing member of the

Table of Contents

- selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (11) Aaron Davis, managing director of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
 - (12) Kevin Kotler has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
 - (13) Bryan Horton, the trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
 - (14) Capital Ventures International (CVI) is affiliated with one or more FINRA members, none of whom are currently expected to participate in the offering and resale pursuant to the prospectus contained in this registration statement of the shares held of record by CVI. Heights Capital Management, Inc., the authorized agent of CVI, has discretionary authority to vote and dispose of the shares held by CVI and may be deemed to be the beneficial owner of these shares. Martin Kobinger, in his capacity as Investment Manager of Heights Capital Management, Inc., may also be deemed to have investment discretion and voting power over the shares held by CVI. Mr. Kobinger disclaims any such beneficial ownership of the shares.
 - (15) Includes the following securities that are not being offered in this offering: (a) 50,000 shares of our common stock held of record by the selling stockholder, and (b) 5,369 shares of our common stock underlying an option held by the selling stockholder and exercisable within 60 days following March 25, 2014. The selling stockholder is and has been since October 31, 2013 a member of our Board of Directors. See the disclosure under the headings Certain Relationships and Related Transactions, Management and Certain Corporate Governance Matters and Executive Compensation for further information about our relationships and transactions with this selling stockholder.
 - (16) Eli Casdin, manager of Casdin Capital, LLC, the investment adviser of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
 - (17) Includes the following securities that are not being offered in this offering: 66,667 shares of our common stock held of record by the selling stockholder.
 - (18) Includes the following securities that are not being offered in this offering: 3,316,618 shares of our common stock held of record by the selling stockholder. Dr. Jonathan E. Lim, our President, Chief Executive Officer and Chairman of our Board of Directors, is the Manager of City Hill Ventures, LLC, which is the Manager of City Hill Ventures Partners I, LLC, and as such he and City Hill Ventures, LLC have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities. Dr. Lim disclaims beneficial ownership of the securities held of record by the selling stockholder except to the extent of his pecuniary interest therein. See the disclosure under the heading Certain Relationships and Related Transactions, Management and Certain Corporate Governance Matters and Executive Compensation for further information about our relationships and transactions with City Hill Ventures Partners I, LLC and Dr. Lim.
 - (19) Fariba Ghodsiar, chief investment officer of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
 - (20) David Freelove, director of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
 - (21) Includes the following securities that are not being offered in this offering: 66,667 shares of our common stock held of record by the selling stockholder. Dan Feldman and Uri Feldman each have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
 - (22) Empery Asset Management LP, the authorized agent of Empery Asset Master, Ltd (EAM), has authority to vote and dispose of the shares held by EAM and may be deemed to be the beneficial owner of these shares. Martin Hoe and Ryan Lane, in their capacity as investment managers of Empery Asset Management LP,

Table of Contents

- may also be deemed to have investment discretion and power over the shares held by EAM. Empery Asset Management LP, Mr. Hoe and Mr. Lane each disclaim any beneficial ownership of these shares.
- (23) James B. Tananbaum, the managing member of the general partner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (24) Fourth Avenue Capital Partners GP LLC is the general partner of Fourth Avenue Capital Partners LP, and as such, Fourth Avenue Capital Partners GP LLC may be deemed to beneficially own the shares held by Fourth Avenue Capital Partners LP. The managing members of Fourth Avenue Capital Partners GP LLC are Daniel Gold, Tracy Fu, Nicholas Brumm and Arthur Chu, each of whom disclaims beneficial ownership of the shares held by Fourth Avenue Capital Partners LP.
- (25) Excludes 16,667 shares of our common stock held of record by Arbco Partners, LP, which are also being offered in this offering. The selling stockholder is the managing partner of Arbco Partners, LP and as such may be deemed to beneficially own the securities that it holds of record.
- (26) Doron Breen, director of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (27) Independence Capital Asset Partners, LLC, the general partner of the selling stockholder, and James A. Hillary and Andrew Kalmar have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (28) Randal L. Wechter, the trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (29) Douglas Kirk Horton, the general partner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (30) Stephen M. Liu, the president of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (31) The selling stockholder is a registered representative of Tripoint Global Equities, a registered broker-dealer.
- (32) Dominique Semon, managing partner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (33) Thomas J. Wynn, partner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (34) Christopher Fuglesang, president of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (35) Andrew M. Kaplan, the Chief Executive Officer of the General Partner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (36) Robert S. Finkelstein has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (37) Robert Aaron Fink, the trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (38) Sabby Management, LLC serves as the investment manager of Sabby Healthcare Volatility Master Fund, Ltd. Hal Mintz is the manager of Sabby Management, LLC. As such, Sabby Management, LLC and Hal Mintz have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities. Each of Sabby Management, LLC and Hal Mintz disclaims beneficial ownership over the securities held of record by the selling stockholder except to the extent of its or his pecuniary interest therein.
- (39) The selling stockholder is a managing director of Ladenburg Thalmann & Co. Inc., which served as the placement agent in the Initial Private Placement and which received approximately \$2.25 million in fees and expense reimbursement in exchange for such placement agent services.

Table of Contents

- (40) Behzad Aghazadeh and Kurt von Emster, portfolio managers of the selling stockholder, have the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (41) Jacob Gottlieb has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities. Mr. Gottlieb disclaims beneficial ownership of such securities except to the extent of his pecuniary interest therein.
- (42) All information regarding investors in the Subsequent Private Placement is provided as of November 29, 2013.
- (43) Don B. Whaley, the manager of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (44) Ann Robbins Cohen, the trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (45) Lindsay A. Rosenwald, M.D., owner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities. Dr. Rosenwald is a 50% owner of Opus Point Partners, LLC, which owns less than 25% of National Holdings Corp., an owner of several registered broker-dealers, including National Securities Corporation, which served as the placement agent in the Subsequent Private Placement and received approximately \$636,000 in fees and expense reimbursement in exchange for such placement agent services.
- (46) Harry M. Farnham III, Chief Secretary and Treasurer of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (47) Includes the following securities that are not being offered in this offering: 83,334 shares of our common stock held of record by the selling stockholder. David A. Ramsay, trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (48) Dr. David Shively, trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (49) Each of Michael Carpentieri, Margaret Defeo, Joseph Mazzocchi and Micahel Falzarano, officers of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (50) Timothy W. Rudolph, President and owner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (51) Excludes 10,000 shares of our common stock held of record by Jastco Mayfair Intl. Property, LLC, which are also being offered in this offering. The selling stockholder is a member of Jastco Mayfair Intl. Property, LLC and as such may be deemed to beneficially own the securities that it holds of record.
- (52) Each of George S. and Barbara L. O Connor, trustees of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (53) Karen Jean Gilmore currently serves, and has served since September 2011, as our controller.
- (54) William G. Glendenning, partner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (55) Excludes 8,000 shares of our common stock held of record by Grant s Engineering and Machine Company, which are also being offered in this offering. The selling stockholder is the owner of Grant s Engineering and Machine Company and as such may be deemed to beneficially own the securities that it holds of record.
- (56) Douglas Grant, owner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.

Table of Contents

- (57) Jacob Lomazow, trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (58) Michael Gunther, Chief Executive Officer of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (59) Jason Fadeyi, member of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (60) Excludes 9,000 shares of our common stock held of record by Sunstone Partners, LLC, which are also being offered in this offering. The selling stockholder is the President of Sunstone Partners, LLC and as such may be deemed to beneficially own the securities that it holds of record.
- (61) Includes the following securities that are not being offered in this offering: 33,334 shares of our common stock held of record by Maung Investment Group, of which the selling stockholder is a partner and as such may be deemed to beneficially own such securities.
- (62) Max G. Johnson, trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (63) The selling stockholder is a broker at National Securities Corporation, a registered broker-dealer that served as the placement agent in the Subsequent Private Placement and received approximately \$636,000 in fees and expense reimbursement in exchange for such placement agent services.
- (64) Philip Emmons, owner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (65) Paul J. Steinle Jr., owner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (66) Each of Gregory M. Reesman and Christopher Michael Reesman has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (67) Rhoda Ann Miller, trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (68) Excludes an aggregate of 50,000 shares of our common stock held of record by Blue Ocean LLC, DJDDT Properties, LLC, Paramount Biosciences, LLC, RAQ LLC and RNW LLC, all of which are also being offered in this offering. The selling stockholder is the owner of each such entity and as such may be deemed to beneficially own the securities that each holds of record. The selling stockholder is a 50% owner of Opus Point Partners, LLC, which owns less than 25% of National Holdings Corp., an owner of several registered broker-dealers, including National Securities Corporation, which served as the placement agent in the Subsequent Private Placement and received approximately \$636,000 in fees and expense reimbursement in exchange for such placement agent services.
- (69) Excludes 8,300 shares of our common stock held of record by Dr. David Shively Rev Dynastic With Preservation Trust, which are also being offered in this offering. The selling stockholder is the trustee of Dr. David Shively Rev Dynastic With Preservation Trust and as such may be deemed to beneficially own the securities that it holds of record.
- (70) Ronald T. Evans, President of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (71) John Maddux, President of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (72) William A. Moore, President of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (73) Each of Scot Evan Ginsberg and Frederica Adam Ginsberg, trustees of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.
- (74) Tony L. Chang, trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.

- (75) Raymond Tsai, trustee of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.

Table of Contents

(76) Arthur Koerner, owner of the selling stockholder, has the power to vote or dispose of the securities held of record by the selling stockholder and may be deemed to beneficially own those securities.

Other than as described in the above table and accompanying footnotes or as described below, (a) we have not made, and are not required to make, any potential payments regarding the Private Placements to any selling stockholder, any affiliate of a selling stockholder, or any person with whom any selling stockholder has a contractual relationship, and (b) other than in connection with the Private Placements, the selling stockholders have not had, and do not have, any material relationship with us except for their ownership of our common stock and other securities as set forth in the above table and related footnotes.

The investors in the Private Placements have ongoing registration rights pursuant to the terms of the Registration Rights Agreement relating to the securities issued and sold to them in the Private Placements. See the more fulsome description of the Registration Rights Agreement set forth under the heading **Description of Securities Registration Rights Agreement** below.

We may be required to make certain payments to the investors in the Private Placements under certain circumstances pursuant to the terms of the applicable Securities Purchase Agreement and the Registration Rights Agreement. These potential payments include (a) potential liquidated damages for certain filing and effectiveness failures relating to our registration of the common stock issued and sold in the Private Placements (provided that such liquidated damages are not to exceed 6.0% of the aggregate subscription amount paid by each investor in the Private Placements), and (b) amounts payable if we or our transfer agent fail to timely remove certain restrictive legends from certificates representing the shares of common stock being offered hereby following the eligibility of such shares for resale under this registration statement or Rule 144 promulgated under the Securities Act. We intend to comply with such requirements of the Securities Purchase Agreements and the Registration Rights Agreement and do not currently expect to make any such payments; however, it is possible that such payments may be required.

The Securities Purchase Agreement we entered into with investors in the Initial Private Placement contains certain anti-dilution provisions, which are not contained in the Securities Purchase Agreement we entered into with the investors in the Subsequent Private Placement. Those anti-dilution provisions provide that, if we issue and sell certain of our equity securities at a purchase price per share lower than \$6.00 within the 180-day period following November 6, 2013, the investors in the Initial Private Placement shall be entitled to receive such number of additional shares of our common stock as they would have received had such lower purchase price per share been applicable in the Initial Private Placement. Certain issuances of our equity securities are not subject to such anti-dilution provisions, including: issuances pursuant to the exercise or conversion of outstanding options, warrants or other convertible securities; issuances in connection with acquisitions, asset purchases, licenses, collaborations or strategic transactions that are not for the primary purpose of raising capital; issuances to our employees, officers, directors, consultants or advisors under stock incentive plans or other arrangements that are approved by our Board of Directors; and issuances that the holders of a majority of the outstanding shares issued in the Initial Private Placement elect in writing to exclude from the application of such provisions.

Table of Contents

PLAN OF DISTRIBUTION

We are registering the shares of common stock issued to the selling stockholders to permit the resale of these shares of common stock by the holders of the shares of common stock from time to time after the date of this prospectus. We will not receive any of the proceeds from the sale by the selling stockholders of the shares of common stock. We will bear all fees and expenses incident to our obligation to register the shares of common stock.

The selling stockholders may sell all or a portion of the shares of common stock beneficially owned by them and offered hereby from time to time directly or through one or more underwriters, broker-dealers or agents. If the shares of common stock are sold through underwriters or broker-dealers, the selling stockholders will be responsible for underwriting discounts or commissions or agent's commissions. The shares of common stock may be sold in one or more transactions, which may involve crosses or block transactions, and may be sold on any national securities exchange or quotation service on which our common stock may be listed or quoted at the time of sale, in the over-the-counter market, or in transactions otherwise than on these exchanges or systems. As of the date of this prospectus, our common stock is listed on the NASDAQ Capital Market under the symbol RXDX. As of March 25, 2014, the last reported sale price of our common stock was \$8.95 per share. Further, sales of the common stock to be registered hereunder could be made at prevailing market prices at the time of the sale, at fixed prices, at negotiated prices, or at varying prices determined at the time of sale. As a result, we cannot know the price at which any of our common stock to be registered hereunder may ultimately be sold by the holders thereof.

The selling stockholders may use any one or more of the following methods when selling shares:

ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;

block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;

purchases by a broker-dealer as principal and resale by the broker-dealer for its account;

an exchange distribution in accordance with the rules of the applicable exchange;

privately negotiated transactions;

settlement of short sales entered into after the effective date of the registration statement of which this prospectus is a part;

broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

through the writing or settlement of options or other hedging transactions, whether such options are listed on an options exchange or otherwise;

a combination of any such methods of sale; and

any other method permitted pursuant to applicable law.

The selling stockholders also may resell all or a portion of the shares in open market transactions in reliance upon Rule 144 under the Securities Act, as permitted by that rule, or Section 4(a)(1) under the Securities Act, if available, rather than under this prospectus, provided that they meet the criteria and conform to the requirements of those provisions.

Broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in sales. If the selling stockholders effect such transactions by selling shares of common stock to or through underwriters, broker-dealers or agents, such underwriters, broker-dealers or agents may receive commissions in the form of discounts, concessions or commissions from the selling stockholders or commissions from

Table of Contents

purchasers of the shares of common stock for whom they may act as agent or to whom they may sell as principal. Such commissions will be in amounts to be negotiated, but, except as set forth in a supplement to this prospectus, in the case of an agency transaction will not be in excess of a customary brokerage commission in compliance with FINRA Rule 5110.

In connection with sales of the shares of common stock or otherwise, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the shares of common stock in the course of hedging in positions they assume. The selling stockholders may also sell shares of common stock short and if such short sale shall take place after the date that this registration statement is declared effective by the SEC, the selling stockholders may deliver shares of common stock covered by this prospectus to close out short positions and to return borrowed shares in connection with such short sales. The selling stockholders may also loan or pledge shares of common stock to broker-dealers that in turn may sell such shares, to the extent permitted by applicable law. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or the creation of one or more derivative securities which require the delivery to such broker-dealer or other financial institution of shares offered by this prospectus, which shares such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction). Notwithstanding the foregoing, the selling stockholders have been advised that they may not use shares registered pursuant to this registration statement to cover short sales of our common stock made prior to the date the registration statement of which this prospectus forms a part is declared effective by the SEC.

The selling stockholders may, from time to time, pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders and any broker-dealer or agents participating in the distribution of the shares of common stock offered hereby may be deemed to be underwriters within the meaning of Section 2(11) of the Securities Act in connection with such sales. In such event, any commissions paid, or any discounts or concessions allowed to, any such broker-dealer or agent and any profit on the resale of the shares purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Selling stockholders who are underwriters within the meaning of Section 2(11) of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act and may be subject to certain statutory liabilities of, including but not limited to, Sections 11, 12 and 17 of the Securities Act and Rule 10b-5 under the Exchange Act.

Each selling stockholder has informed us that it is not a registered broker-dealer and does not have any written or oral agreement or understanding, directly or indirectly, with any person to distribute the common stock. Upon us being notified in writing by a selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of common stock through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker-dealer, a supplement to this prospectus will be filed, if required, pursuant to Rule 424(b) under the Securities Act, disclosing (i) the name of each such selling stockholder and of the participating broker-dealer(s), (ii) the number of shares involved, (iii) the price at which such the shares of common stock were sold, (iv) the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable, (v) that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and (vi) other facts material to the transaction. In no event shall any broker-dealer receive

fees, commissions and markups, which, in the aggregate, would exceed eight percent (8%).

Table of Contents

Under the securities laws of some states, the shares of common stock may be sold in such states only through registered or licensed brokers or dealers. In addition, in some states the shares of common stock may not be sold unless such shares have been registered or qualified for sale in such state or an exemption from registration or qualification is available and is complied with in all respects.

Any selling stockholder may sell some, all or none of the shares of common stock to be registered pursuant to the registration statement of which this prospectus forms a part.

Each selling stockholder and any other person participating in such distribution will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including, without limitation, Regulation M of the Exchange Act, which may limit the timing of purchases and sales of any of the shares of common stock by the selling stockholder and any other participating person. Regulation M may also restrict the ability of any person engaged in the distribution of the shares of common stock to engage in market-making activities with respect to the shares of common stock. All of the foregoing may affect the marketability of the shares of common stock and the ability of any person or entity to engage in market-making activities with respect to the shares of common stock.

We will pay all expenses of the registration of the shares of common stock pursuant to the Registration Rights Agreement, including, without limitation, SEC filing fees and expenses of compliance with state securities or blue sky laws; provided, however, that each selling stockholder will pay all underwriting discounts and selling commissions, if any, and any legal expenses incurred by it. We will indemnify the selling stockholders against certain liabilities, including some liabilities under the Securities Act, in accordance with the Registration Rights Agreement, or the selling stockholders will be entitled to contribution. We may be indemnified by the selling stockholders against civil liabilities, including liabilities under the Securities Act, that may arise from any written information furnished to us by the selling stockholders specifically for use in this prospectus, in accordance with the Registration Rights Agreement, or we may be entitled to contribution.

Table of Contents

DETERMINATION OF OFFERING PRICE

The selling stockholders will determine at what price they may sell the shares of common stock offered by this prospectus, and such sales may be made at fixed prices, at prevailing market prices at the time of the sale, at varying prices determined at the time of sale, or at negotiated prices. On March 25, 2014, the last reported sale price of our common stock on the NASDAQ Capital Market was \$8.95 per share.

Table of Contents

USE OF PROCEEDS

We will not receive any proceeds from the sale of our common stock offered by this prospectus. We have agreed to bear the expenses (other than any underwriting discounts or selling commissions or any legal expenses incurred by any selling stockholder) in connection with the registration of the shares of our common stock being offered for resale hereunder by the selling stockholders.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

The following describes the material terms of our capital stock. The following description does not purport to be complete and is subject to, and qualified in its entirety by reference to, our Amended and Restated Articles of Incorporation and Bylaws, which are attached as Exhibits 3.1 and 3.2, respectively, to the registration statement of which this prospectus forms a part. All of our stockholders are urged to read our Amended and Restated Articles of Incorporation and Bylaws carefully and in their entirety.

Authorized Capital Stock; Issued and Outstanding Capital Stock

Effective October 31, 2013, we amended and restated our Articles of Incorporation to increase our authorized common stock, par value \$0.00001 per share, from 25,000,000 shares to 100,000,000 shares and to authorize 10,000,000 shares of preferred stock, par value \$0.00001 per share.

Also on October 31, 2013, in connection with the merger in which Ignyta Operating became our wholly owned subsidiary and pursuant to our Amended and Restated Articles of Incorporation, we effected a reverse stock split at a ratio of 100-to-one, such that each 100 shares of our common stock issued and outstanding immediately prior to the effective time of the reverse stock split were automatically combined and converted, without any action on the part of the stockholder thereof, into one fully paid and nonassessable share of our common stock. All share information in this prospectus gives retroactive effect to that reverse stock split. Also on October 31, 2013 and immediately following the effect of the reverse stock split, we declared a \$3.50 per share cash dividend to our stockholders of record and repurchased 80,000 shares of our common stock at a price of \$0.99 per share from our principal stockholder, each on a post reverse stock split basis.

As of March 25, 2014, there were a total of 19,575,144 shares of our common stock issued and outstanding and no shares of preferred stock issued and outstanding.

Common Stock

All of the securities being offered pursuant to the registration statement of which this prospectus is a part are shares of our common stock. The holders of our common stock are entitled to one vote per share on all matters submitted to vote of our stockholders, including the election of directors. Holders of our common stock are not entitled to cumulate their votes for the election of directors. Except as otherwise required by law, or as otherwise fixed by resolution or resolutions of our Board of Directors with respect to one or more series of our preferred stock, the entire voting power and all voting rights shall be vested exclusively in our common stock.

Holders of our common stock will not be entitled to receive dividends except if declared by our Board of Directors and will not be entitled to a liquidation preference in respect of their shares of common stock. Upon liquidation, dissolution or winding up of our company, the holders of our common stock will be entitled to receive pro rata all assets remaining for distribution to stockholders after the payment of all of our liabilities and of all preferential amounts to which any series of our preferred stock may be entitled.

Holders of our common stock will have no preemptive or subscription rights, and will have no rights to convert their common stock into any other securities. The common stock will not be subject to call or redemption.

Preferred Stock

Our Amended and Restated Articles of Incorporation authorize our Board of Directors to fix or alter the dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and dissolution preferences or any wholly unissued series of our preferred stock, and the number of shares constituting any such series and the designation thereof, or any of them. Our Amended and Restated Articles of Incorporation also provide that our Board of Directors is expressly

Table of Contents

authorized to increase or decrease (but not below the number of shares of such series of preferred stock then outstanding) the number of shares of any series of preferred stock subsequent to the issue of shares of that series.

Anti-Takeover Provisions

Nevada law contains provisions governing the combination of a Nevada corporation with 200 or more stockholders of record with an interested shareholder (a person who is the direct or indirect beneficial owner of 10% or more of the voting power of the outstanding voting shares of a corporation), which generally prohibit such transaction for three years following the time that such person becomes an interested shareholder, subject to certain exceptions. Generally, such provisions may have the effect of delaying or making it more difficult to effect a change in control of our company. Pursuant to our Amended and Restated Articles of Incorporation, we have elected to opt out of these provisions, which will permit us to engage in such transactions with interested shareholders.

Nevada law also contains provisions governing acquisition of a controlling interest of a Nevada corporation. These provisions generally provide that any person or entity that acquires a certain percentage of the outstanding voting shares of a Nevada corporation may be denied voting rights with respect to the acquired shares, unless the holders of a majority of the voting power of the corporation, excluding shares as to which any of such acquiring person or entity, an officer or a director of the corporation, and an employee of the corporation exercises voting rights, elect to restore such voting rights in whole or in part. These provisions apply whenever a person or entity acquires shares that, but for the operation of these provisions, would bring voting power of such person or entity in the election of directors within any of the following three ranges: (i) 20% or more but less than 33 1/3%; (ii) 33 1/3% or more but less than or equal to 50%; or (iii) more than 50%. The stockholders or board of directors of a corporation may elect to exempt the stock of the corporation from these provisions through adoption of a provision to that effect in its articles of incorporation or bylaws. Our Amended and Restated Articles of Incorporation and Bylaws do not exempt our common stock from these provisions. These provisions are applicable only to a Nevada corporation that: (i) has 200 or more stockholders of record, at least 100 of whom have addresses in Nevada appearing on the stock ledger of the corporation; and (ii) does business in Nevada directly or through an affiliated corporation. As a result, we do not presently believe that Nevada's controlling interest acquisition provisions are currently applicable to us.

Our Amended and Restated Articles of Incorporation and Bylaws may delay or discourage transactions involving an actual or potential change of control of our company or change in our Board of Directors, including transactions in which our stockholders might otherwise receive a premium for their shares of our common stock, or transactions that our stockholders might otherwise deem to be in their best interests. Therefore, these provisions could adversely affect the price of our common stock. Among other things, our Amended and Restated Articles of Incorporation and Bylaws and applicable Nevada law:

permit our Board of Directors to issue up to 10,000,000 shares of preferred stock, with any rights, preferences and privileges as they may designate (including dividend rights, dividend rate, conversion rights, voting rights, rights and terms of redemption (including sinking fund provisions), redemption price or prices, and dissolution preferences);

provide that, subject to the rights of any series of preferred stock to elect directors, directors may only be removed, subject to any limitation imposed by law, by the holders of at least 2/3 of the voting power of all of our then-outstanding shares of the capital stock entitled to vote generally at an election of directors;

provide that all vacancies, including newly created directorships, may, except as otherwise required by law, be filled by a vote of a majority of directors then in office; and

do not provide for cumulative voting rights (therefore allowing the holders of a majority of the shares of common stock entitled to vote in any election of directors to elect all of the directors standing for election, if they should so choose).

Table of Contents

The amendment of any of these provisions would require approval by the majority of our Board of Directors or by the holders of at least a majority of the voting power of all of our then-outstanding common stock entitled to vote, voting together as a single class.

Warrants

SVB Warrants

In connection with the loan and security agreement between Ignyta Operating and SVB, under which we have become a co-borrower and guarantor, Ignyta Operating issued to SVB two warrants to acquire shares of its capital stock. The first such warrant was issued on June 25, 2012, has a term of exercise of seven years, and, as of immediately prior to the closing of the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary, provided for the purchase by SVB of up to 8,334 shares of Ignyta Operating's series B preferred stock at an exercise price of \$3.00 per share. The second such warrant was issued on February 27, 2013 and became issuable for an increased number of shares on July 19, 2013, has a term of exercise of seven years, and, as of immediately prior to the closing of such merger, provided for the purchase by SVB of up to 16,667 shares of Ignyta Operating's series B preferred stock at an exercise price of \$3.00 per share. The terms of each such warrant provide for anti-dilution and other adjustments in the event of certain stock dividends, stock splits, recapitalizations, reclassifications and consolidations.

In connection with the conversion of all issued and outstanding shares of all series of Ignyta Operating's preferred stock and, immediately thereafter, the reverse stock split of all issued and outstanding shares of Ignyta Operating's common stock, immediately prior to the closing of the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary the warrants issued to SVB converted into, in the aggregate, a right to acquire up to 25,001 shares of Ignyta Operating's common stock at an exercise price per share equal to \$3.00. Upon the closing of the merger, pursuant to and in accordance with the terms and provisions of the warrants and the merger agreement entered into in connection with the merger, such warrants were assumed by us and have become exercisable for up to 25,001 shares of our common stock at an exercise price of \$3.00 per share. Upon exercise, the aggregate exercise price of each of the warrants issued to SVB may be paid by cash or, at the option of SVB, through a customary cashless exercise process. The warrants issued to SVB are attached as exhibits to the registration statement of which this prospectus forms a part and are incorporated herein by reference.

NMS Warrant

Pursuant to the terms of the license agreement between Ignyta Operating and NMS, on November 6, 2013, we issued to NMS a warrant to acquire up to 16,667 shares of our common stock. That warrant has an exercise price of \$6.00 per share and is exercisable at the option of the holder, in whole or in part, at any time until November 6, 2018. The terms of such warrant provide for adjustments in the event of certain stock dividends, stock splits, recapitalizations, reclassifications and consolidations. Upon exercise, the aggregate exercise price of the warrant issued is payable by NMS in cash. The warrant issued to NMS is attached as an exhibit to the registration statement of which this prospectus forms a part and is incorporated herein by reference.

Registration Rights Agreement

In November 2013, we entered into a registration rights agreement with the investors that participated in private placements of our common stock. Pursuant to the terms of the registration rights agreement, on December 19, 2013 we filed with the SEC a registration statement to register for resale all of the 9,010,238 shares of our common stock issued in such private placements, which registration statement was subsequently declared effective by the SEC on February 11, 2014.

Table of Contents

Under the registration rights agreement, subject to exception in certain circumstances, we have agreed to keep such registration statement effective until the later of November 6, 2014 and such time as all of the securities to be registered thereunder have been sold or may be sold without restriction pursuant to Rule 144. If there is not an effective registration statement covering the resale of the securities to be registered thereunder at any time during the period required by the registration rights agreement, then the selling stockholders will have piggyback registration rights with respect to any such securities that are not eligible for resale pursuant to Rule 144 in connection with any other registration statement we file that would permit the inclusion of those shares.

The foregoing description of the registration rights agreement does not purport to be complete, and is qualified in its entirety by the complete text of that agreement, which is attached as an exhibit to the registration statement of which this prospectus forms a part and is incorporated herein by reference.

Transfer Agent

The transfer agent for our securities is Olde Monmouth Stock Transfer Co., Inc., whose address is 200 Memorial Parkway, Atlantic Highlands, New Jersey 07716, and whose telephone number is (732) 872-2727.

Exchange Listing

Our common stock is listed on the NASDAQ Capital Market under the symbol **RXDX**.

Liability and Indemnification of Directors and Officers

The Nevada Revised Statutes empower us to indemnify our directors and officers against expenses relating to certain actions, suits or proceedings as provided for therein. In order for such indemnification to be available, the applicable director or officer must not have acted in a manner that constituted a breach of his or her fiduciary duties and involved intentional misconduct, fraud or a knowing violation of law, or must have acted in good faith and reasonably believed that his or her conduct was in, or not opposed to, our best interests. In the event of a criminal action, the applicable director or officer must not have had reasonable cause to believe his or her conduct was unlawful.

Under applicable provisions of the Nevada Revised Statutes, our articles of incorporation, bylaws or any separate agreement may provide for our payment of expenses incurred by any such director or officer in advance of the final disposition of the applicable action, suit or proceeding, upon delivery by such director or officer of an undertaking to repay all amounts so advanced if it is ultimately determined that the director or officer is not entitled to be indemnified by us.

Our Amended and Restated Articles of Incorporation provide for indemnification of our directors and officers substantially identical in scope to that permitted under applicable Nevada law. Our Amended and Restated Articles of Incorporation also provide that the expenses of our directors and officers incurred in defending any applicable action, suit or proceeding must be paid by us as they are incurred and in advance of the final disposition of the action, suit or proceeding, provided that the required undertaking by the director or officer is delivered to us.

We have also entered into separate indemnification agreements with each of our current directors and executive officers consistent with Nevada law and in the form approved by our Board of Directors and our stockholders, and we contemplate entering into such indemnification agreements with directors and certain executive officers that may be elected or appointed in the future. Those indemnification agreements require that under the circumstances and to the extent provided for therein, we indemnify such persons to the fullest extent permitted by applicable law against certain expenses incurred by any such person as a result of such person being

Table of Contents

made a party to certain actions, suits and proceedings by reason of the fact that such person is or was a director, officer, employee or agent of our company, any entity that was a predecessor corporation of our company or any of our affiliates. The rights of each person who is a party to such an indemnification agreement are in addition to any other rights such person may have under applicable Nevada law, our Amended and Restated Articles of Incorporation, our Bylaws, any other agreement, a vote of our stockholders, a resolution adopted by our Board of Directors or otherwise. The foregoing is only a brief description of the form of indemnification agreement, does not purport to be a complete description of the rights and obligations of the parties thereunder and is qualified in its entirety by reference to the form of indemnification agreement filed as an exhibit to the registration statement of which this prospectus forms a part and incorporated herein by reference.

We also maintain a customary insurance policy that indemnifies our directors and officers against various liabilities, including liabilities arising under the Securities Act, that may be incurred by any director or officer in his or her capacity as such.

At present, there is no pending litigation or proceeding involving any of our directors or officers for which indemnification is sought, nor are we aware of any threatened litigation that is likely to result in claims for indemnification.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted for our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event a claim for indemnification against such liabilities (other than payment by us for expenses incurred or paid by a director, officer or controlling person of ours in successful defense of any action, suit, or proceeding) is asserted by a director, officer or controlling person in connection with the securities being registered, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction, the question of whether such indemnification by it is against public policy in the Securities Act and will be governed by the final adjudication of such issue.

Table of Contents

**MARKET PRICE OF AND DIVIDENDS ON OUR COMMON
STOCK AND RELATED STOCKHOLDER MATTERS**

Our common stock is listed on the NASDAQ Capital Market under the ticker symbol RXDX. On March 25, 2014, the last reported sale price of our common stock was \$8.95 per share. Our common stock was quoted on the OTCQB Marketplace, or the OTCQB, and the OTC Bulletin Board between December 2, 2013 and March 14, 2014, when our common stock was first listed on the NASDAQ Capital Market. There was no trading of our common stock on any other market, exchange or quotation system before December 2013. Although our common stock is listed on the NASDAQ Capital Market and has been quoted on the OTCQB, there has been a limited trading market for our common stock to date. Because our common stock has been thinly traded, any reported sale prices may not be a true market-based valuation of our common stock.

The table below sets forth reported high and low closing sale prices for our common stock for the fiscal quarters indicated as reported on the OTCQB (for the period prior to March 14, 2014) and the NASDAQ Capital Market (for the period beginning on March 14, 2014).

	High	Low
Fiscal Year Ended December 31, 2012		
Quarter ended March 31, 2012*		
Quarter ended June 30, 2012*		
Quarter ended September 30, 2012*		
Quarter ended December 31, 2012*		
Fiscal Year Ended December 31, 2013		
Quarter ended March 31, 2013*		
Quarter ended June 30, 2013*		
Quarter ended September 30, 2013*		
Quarter ended December 31, 2013	\$ 7.00	\$ 0.01
Fiscal Year Ending December 31, 2014		
Quarter ending March 31, 2014 (through March 25, 2014)	\$ 20.00	\$ 7.00

* There was no market for our common stock during this period.

 Holders

As of March 25, there were 229 holders of record of our common stock.

 Dividends

In connection with and prior to the closing of the merger in which Ignyta Operating became our wholly owned subsidiary, on October 31, 2013, we declared a \$3.50 per share cash dividend to our common stockholders of record as of that date and time. Other than the dividend declared in connection with the merger, we have never declared nor paid any cash dividends to stockholders. We do not intend to pay cash dividends on our common stock for the foreseeable future, and currently intend to retain any future earnings to fund our operations and the development and growth of our business. The declaration of any future cash dividend, if any, would be at the discretion of our Board of

Directors and would depend upon our earnings, if any, our capital requirements and financial position, our general economic conditions, and other pertinent conditions. In addition, our ability to pay cash dividends is currently prohibited by the terms of our loan agreement with SVB.

Table of Contents**MANAGEMENT'S DISCUSSION AND ANALYSIS OF
FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with Selected Consolidated Financial Data and our consolidated financial statements and related notes appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business, includes forward-looking statements that involve risks and uncertainties as described under the heading Special Note Regarding Forward-Looking Statements elsewhere in this prospectus. You should review the disclosure under the heading Risk Factors in this prospectus for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

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

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

Overview

We were incorporated under the laws of the State of Delaware on August 29, 2011 with the name NexDx, Inc. We changed our name to Ignyta, Inc. on October 8, 2012. On October 31, 2013, a wholly owned subsidiary of Ignyta merged with and into our company, pursuant to which we became the wholly owned subsidiary of Ignyta. We changed our name to Ignyta Operating, Inc. in connection with the closing of the merger. On October 31, 2013, prior to the closing of the merger, (i) all then-outstanding shares of each series of our preferred stock were voluntarily converted by the holders thereof into shares of our common stock in accordance with our certificate of incorporation, and (ii) we effected a three-to-one reverse stock split of our issued and outstanding shares of capital stock. All share information in this discussion and analysis relating to our capital stock gives retroactive effect to that reverse stock split. On May 20, 2013, we completed our acquisition of Actagene Oncology, Inc., or Actagene, which merged with and into our company on that date.

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

Table of Contents

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 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 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.

Since inception, our operations have focused on organizing and staffing our company, business planning, raising capital, assembling our core capabilities in genetic and epigenetic based biomarker and drug target discovery, identifying potential product candidates and developing such candidates. Our product candidate development operations include preparing, managing and conducting preclinical and clinical studies and trials, preparing regulatory submissions relating to those product candidates and establishing and managing relationships with third parties in connection with all of those activities. We expect that in the future our operations may also, if regulatory approval is obtained, include pursuing the commercialization of our product candidates. To date, we have financed our operations primarily through funding received from private placement offerings of our capital stock and under a loan agreement. We have had no revenue to date. Since our inception and through December 31, 2013, we have raised an aggregate of approximately \$70 million to fund our operations, of which approximately \$60 million has been received from our issuance and sale of our equity securities and \$10.0 million has been received under our loan and security agreement with SVB.

Since inception, we have incurred significant operating losses. Our net losses were \$14.2 million, \$1.3 million and \$15.6 million for the periods ended December 31, 2013 and 2012 and for the period from August 29, 2011 (inception) through December 31, 2013, respectively. As of December 31, 2013, we had an accumulated deficit of \$15.6 million. We expect to continue to incur significant expenses and operating losses over the next several years. Our net losses may fluctuate significantly from quarter to quarter and from year to year. We anticipate that our expenses will increase significantly now that we have assumed financial responsibility for the ongoing and any future studies and trials of RXDX-101 and as we plan for the commencement of potential Phase II clinical development activities for RXDX-101; pursue the initial stages of development of our Spark-1, Spark-2 and Spark-3 programs; continue to discover, validate and develop additional novel product candidates; expand and protect our intellectual property portfolio; and hire additional scientific, business, accounting and financial personnel. In addition, we expect to incur additional costs associated with operating as a public company.

Financial Operations Overview*Revenue*

To date, we have not generated any revenue from product sales or otherwise, and do not expect to generate any revenue from the sale of products in the near future.

In the future, we expect that we will seek to generate revenue primarily from product sales, but may also seek to generate revenue from research funding, milestone payments and royalties on future product sales in connection with any out-license or other strategic relationships we may establish.

Table of Contents*Research and Development Expenses*

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

license fees;

employee-related expenses, including salaries, benefits and stock-based compensation expense;

expenses incurred under agreements with third parties, including consultants and advisors we engage for research-related services and any CROs that we may engage in connection with conducting preclinical and clinical activities on our behalf;

the cost of laboratory supplies; and

facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance and other operating costs.

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

We have not yet begun tracking our internal and external research and development costs on a program-by-program basis. As such, we do not have historical research and development expenditures by program and we use our employee and infrastructure resources across multiple research and development programs. The following table sets forth our research and development expenses for the periods presented:

	Year ended December 31,	
	2013	2012
Total research and development expenses	\$ 10,170,866	\$ 708,043

Research and development activities are central to our business model. Our research and development programs that we expect will be our focus in the immediate future consist of the development of RXDX-101, for which we acquired exclusive development rights upon the effectiveness of our license agreement with NMS on November 6, 2013, and drug discovery activities for the development of our Spark-1, Spark-2 and Spark-3 programs. All of those research and development programs are in the early stage, and since product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials, we expect research and development costs relating to each of those programs to increase significantly for the foreseeable future. However, the successful development of any of those product candidates, or any others we may seek to pursue, is highly uncertain. As such, at this time, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the remainder of the development of these product candidates, or whether any of these product candidates will reach

successful commercialization. We are also unable to predict when, if ever, any net cash inflows will commence from any of the product candidates we currently or may in the future pursue. This lack of predictability is due to the numerous risks and uncertainties associated with developing medicines, many of which, such as our ability to obtain approvals to market and sell those medicines from the FDA and other applicable regulatory authorities, are beyond our control, including the uncertainty of:

establishing an appropriate safety profile with toxicology studies adequate to submit to the FDA in an investigational new drug application, or IND, or comparable applications to foreign regulatory authorities;

successful enrollment in and adequate design and completion of clinical trials;

Table of Contents

receipt of marketing approvals from applicable regulatory authorities, including the FDA and comparable foreign authorities;

establishing commercial manufacturing capabilities or, more likely, seeking to establish arrangements with third-party manufacturers;

obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our product candidates;

launching commercial sales of the products, if and when approved, including establishing an internal sales and marketing force or establishing relationships with third parties for such purpose;

developing and commercializing, individually or with third-party collaborators, companion diagnostics; and

a continued acceptable safety profile of the products following approval, if any.

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

General and Administrative Expenses

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

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

Critical Accounting Policies and Estimates

This discussion and analysis of our financial condition and results of operations are based on our consolidated financial statements, which we have prepared in accordance with United States generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates, judgments and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported amounts of expenses during the reporting periods. We base our estimates on historical experience and on various other factors and assumptions that we believe are reasonable under the circumstances at the time the estimates are made, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources.

Actual results may differ from these estimates under different assumptions or conditions. We periodically evaluate our estimates and judgments, including those described in greater detail below, in light of changes in circumstances, facts and experience.

Table of Contents

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

Revenue Recognition

To date, we have not generated any revenue.

Income Taxes

Deferred income taxes are recognized for the tax consequences in future years of differences between the tax basis of assets and liabilities and their financial reporting amounts at each year end based on enacted tax laws and statutory tax rates applicable to the periods in which the differences are expected to affect taxable income. Valuation allowances are established when necessary to reduce deferred tax assets to the amount expected to be realized. Income tax expense is the combination of the tax payable for the year and the change during the year in deferred tax assets and liabilities.

Cash and Cash Equivalents

We consider all highly liquid investments with an original maturity of 90 days or less when purchased to be cash equivalents. Cash equivalents primarily represent amounts invested in money market funds whose cost equals market value.

Stock-Based Compensation

We account for stock-based compensation in accordance with Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 718, *Compensation Stock Compensation*, which establishes accounting for equity instruments exchanged for employee services. Under such provisions, stock-based compensation cost is measured at the grant date, based on the calculated fair value of the award, and is recognized as an expense, under the straight-line method, over the employee's requisite service period (generally the vesting period of the equity grant).

We account for equity instruments, including restricted stock or stock options, issued to non-employees in accordance with authoritative guidance for equity based payments to non-employees. Stock options issued to non-employees are accounted for at their estimated fair value determined using the Black-Scholes option-pricing model. The fair value of options granted to non-employees is re-measured as they vest, and the resulting increase in value, if any, is recognized as expense during the period the related services are rendered. Restricted stock issued to non-employees is accounted for at their estimated fair value as they vest.

Derivative Liabilities

We account for our warrants as either equity or liabilities based upon the characteristics and provisions of each instrument. Warrants classified as derivative liabilities are recorded on our balance sheet at their fair value on the date of issuance and revalued on each subsequent balance sheet date until such instruments are exercised or expire, with any changes in the fair value between reporting periods recorded as other income or expense. We estimate the fair

value of these liabilities using option pricing models and assumptions that are based on the individual characteristics of the warrants or instruments on the valuation date, as well as assumptions for future events, expected volatility, expected life, yield and risk-free interest rate.

Table of Contents

Recently Issued Accounting Pronouncements

There are no recent accounting pronouncements likely to have a material impact on the financial statements.

Emerging Growth Company and Smaller Reporting Company Status

The JOBS Act establishes a class of company called an emerging growth company, which generally is a company whose initial public offering was completed after December 8, 2011 and had total annual gross revenues of less than \$1 billion during its most recently completed fiscal year. Additionally, Section 12b-2 of the Exchange Act establishes a class of company called a smaller reporting company, which generally is a company with a public float of less than \$75 million as of the last business day of its most recently completed second fiscal quarter or, if such public float is \$0, had annual revenues of less than \$50 million during the most recently completed fiscal year for which audited financial statements are available. We currently qualify as both an emerging growth company and a smaller reporting company.

As an emerging growth company and a smaller reporting company, we are eligible to take advantage of certain extended accounting standards and exemptions from various reporting requirements that are not available to public reporting companies that do not qualify for those classifications, including without limitation the following:

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

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

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

Neither an emerging growth company nor a smaller reporting company is required to comply with the requirement of auditor attestation of internal controls over financial reporting, which is required for other public reporting companies by Section 404 of the Sarbanes-Oxley Act of 2002.

A company that is either an emerging growth company or a smaller reporting company is eligible for reduced disclosure obligations regarding executive compensation in its periodic and annual reports, including without limitation exemption from the requirement to provide a compensation discussion and analysis describing compensation practices and procedures.

A company that is either an emerging growth company or a smaller reporting company is eligible for reduced financial statement disclosure in registration statements, which must include two years of audited financial statements rather than the three years of audited financial statements that are required for other public reporting companies. Smaller reporting companies are also eligible to provide such reduced financial statement disclosure in annual reports on Form 10-K.

For as long as we continue to be an emerging growth company and/or a smaller reporting company, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of those

Table of Contents

respective classifications. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year following the fifth anniversary of the date of the first sale of our common stock pursuant to an effective registration statement under the Securities Act, which was on February 15, 2013; (ii) the last day of the fiscal year in which we have total annual gross revenues of \$1 billion or more; (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under applicable SEC rules. We expect that we will remain an emerging growth company for the foreseeable future, but cannot retain our emerging growth company status indefinitely and will no longer qualify as an emerging growth company on or before December 31, 2018. We will remain a smaller reporting company until we have a public float of \$75 million or more as of the last business day of our most recently completed second fiscal quarter, and we could retain our smaller reporting company status indefinitely depending on the size of our public float.

Results of Operations*Comparison of Years Ended December 31, 2013 and 2012*

The following table summarizes our results of operations for the years ended December 31, 2013 and 2012, together with the changes in those items in dollars and as a percentage:

	Year ended December 31,		Dollar change	% change
	2013	2012		
	<i>(in thousands)</i>			
Revenue	\$	\$	\$	%
Operating expenses:				
Research and development	10,171	708	9,463	1,337
General and administrative	3,731	548	3,183	581
Loss from operations	(13,902)	(1,256)	(12,646)	1,007
Other income (expense)	(310)	(23)	(287)	1,247
Provision for income taxes	2	1	1	100
Net loss	\$ (14,214)	\$ (1,280)	\$ (12,934)	1,010%

Revenue. We did not record any revenue for the years ended December 31, 2013 and 2012.

Research and Development Expense. Research and development expense increased by approximately \$9.5 million to approximately \$10.2 million for the year ended December 31, 2013 from approximately \$708,000 for the year ended December 31, 2012, an increase of 1,337%. The increase in research and development expenses was primarily attributable to the upfront license fee of \$7.0 million that we paid to NMS in association of our license of RXDX-101 and RXDX-102, as well as an increase in activities relating to development of these product candidates and our biomarker discovery programs and platform technologies. We also incurred an increase between periods for personnel expenses related to hiring and engaging additional employees and consultants to help us advance our product candidates and facilities related expenses due to the expansion of our leased facilities.

General and Administrative Expense. General and administrative expenses increased by approximately \$3.2 million to approximately \$3.7 million for the year ended December 31, 2013 from approximately \$548,000 for the year ended

December 31, 2012, an increase of 581%. The increase in general and administrative expenses was primarily attributable to increases in personnel costs and investor relations, audit, legal and intellectual property costs, some of which resulted from activities relating to completion of our license agreement with NMS for development rights to RXDX-101 and RXDX-102 and completion of our October 31, 2013 merger, and facilities related expenses.

Table of Contents

Other Income (Expense). Other expense increased by approximately \$287,000 to approximately \$310,000 for the year ended December 31, 2013, from approximately \$23,000 for the year ended December 31, 2012. The increase in other expense was attributable to increased interest owed under our loan agreement with SVB and various loan fees attributable to this debt that were paid off in 2013, as well as the change in the fair value of the warrant liability associated with the SVB warrants.

Liquidity and Capital Resources*Sources of Liquidity*

Since our inception, and through December 31, 2013, we raised an aggregate of approximately \$70 million to fund our operations, of which approximately \$54 million was received from our issuance and sale of our common stock in two private placements in November 2013, \$6 million was received from our issuance and sale of our preferred stock and \$10.0 million was received from the incurrence of indebtedness under our loan agreement with SVB. As of December 31, 2013, we had also received a small amount of funding from our issuance of common stock upon the exercise from time to time of stock options, and from our issuance of common stock to our founders in August and September 2011. As of December 31, 2013, we had approximately \$52 million in cash and cash equivalents.

New Loan Agreement with SVB. On December 31, 2013, we entered into our new loan agreement with SVB and received the funding of the full \$10.0 million principal amount thereunder. The loan agreement replaced our prior loan agreement with SVB, which had a principal amount of \$1.5 million that was replaced by the advance of the principal amount under the new loan agreement. The amount loaned to us under the new loan agreement bears interest at a rate of 6.92%, and is payable in 36 equal monthly installments commencing after a 12-month period of interest-only payments, such that all amounts owed under the new loan agreement will mature on December 1, 2017. Upon such maturity date, we will also owe to SVB a final payment of \$1,050,000, equal to 10.50% of the full principal amount under the new loan agreement. Pursuant to the new loan agreement, we are bound by certain affirmative and negative covenants setting forth actions that we must and must not take during the term thereof, and, all amounts owed thereunder will begin to bear interest at a rate of 11.92% and could be declared due and payable by SVB upon the occurrence of an event of default.

Private Placements. On November 1, 2013, we entered into a securities purchase agreement with 52 accredited investors providing for the issuance and sale to such investors of an aggregate of 7,740,142 shares of our common stock in a private placement, which closed on November 6, 2013. On November 27, 2013, we entered into a securities purchase agreement with 195 accredited investors providing for the issuance and sale to such investors of an aggregate of 1,270,096 shares of our common stock in a subsequent private placement, which closed on November 29, 2013. All shares issued in the private placements were sold at a purchase price per share of \$6.00, for aggregate gross proceeds of approximately \$54.1 million and aggregate net proceeds, after deducting for placement agent and other offering fees and expenses, of approximately \$51.0 million. The securities purchase agreement entered into in connection with the private placement on November 6, 2013 contains certain anti-dilution provisions providing that if we issue and sell certain of our equity securities at a purchase price per share lower than \$6.00 within the 180-day period following November 6, 2013, the investors in the private placement shall be entitled to receive such number of additional shares of our common stock as they would have received had such lower purchase price per share been applicable in the private placement. Certain issuances of our equity securities are not subject to these anti-dilution provisions, including: issuances pursuant to the exercise or conversion of outstanding options, warrants or other convertible securities; issuances in connection with acquisitions, asset purchases, licenses, collaborations or strategic transactions that are not for the primary purpose of raising capital; issuances to our employees, officers, directors, consultants or advisors under stock incentive plans or other arrangements that are approved by our Board of Directors; and issuances that the holders of a majority of the outstanding shares issued in the private placement elect in writing to exclude from

the application of such provisions.

Table of Contents

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

Cash Flows

The following table provides information regarding our cash flows for the years ended December 31, 2013 and 2012:

	Year ended, December 31,	
	2013	2012
	<i>(in thousands)</i>	
Net cash (used in) operating activities	\$ (13,073)	\$ (991)
Net cash (used in) investing activities	(678)	(306)
Net cash provided by financing activities	60,522	6,173
Net increase (decrease) in cash and cash equivalents	\$ 46,771	\$ 4,876

Net Cash Used in Operating Activities. The use of cash in all periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was approximately \$13.1 million during the year ended December 31, 2013 compared to approximately \$991,000 during the year ended December 31, 2012. The increase in cash used in operating activities during 2013 was driven primarily by an increase in net loss during 2013 as compared to 2012.

Net Cash Used in Investing Activities. Net cash used in investing activities was approximately \$678,000 during the year ended December 31, 2013 compared to approximately \$306,000 during the year ended December 31, 2012. The cash used in investing activities was primarily the result of purchases of fixed assets.

Net Cash Provided by Financing Activities. Net cash provided by financing activities was approximately \$60.5 million during the year ended December 31, 2013 compared to approximately \$6.2 million during the year ended December 31, 2012. The cash provided by financing activities for year ended December 31, 2013 was primarily the result of our November 2013 private placements of common stock and our December 2013 loan transaction with SVB. The cash provided by financing activities during the year ended December 31, 2012 was the result of the issuance and sale of our series A preferred stock in March 2012, resulting in gross proceeds of \$250,000, and the issuance and sale of our series B preferred stock in June 2012 and December 2012, collectively resulting in gross proceeds of approximately \$5.5 million, and the incurrence of indebtedness under our prior loan agreement with SVB in June 2012, resulting in gross proceeds of \$500,000.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly now that we have assumed rights to, and operational and financial responsibility for, the development and manufacturing of RXDX-101 and as

we continue the research and development of, initiate or continue, as applicable, clinical trials of, and seek marketing approval for, those product candidates and our Spark-1, Spark-2 and Spark-3 programs. In addition, if we obtain marketing approval for any of our product candidates in the future, which we anticipate would not occur for several years if at all, we expect we would then incur significant commercialization expenses

Table of Contents

related to product sales, marketing, manufacturing and distribution to the extent that such sales, marketing and distribution are not the responsibility of any collaborators with whom we may engage. Further, we expect to incur additional costs associated with operating as a public company.

In November 2013, we completed two private placements, pursuant to which we issued and sold an aggregate of 9,010,238 shares of our common stock at a price per share of \$6.00 for aggregate net proceeds, after deducting for placement agent and other offering fees and expenses, of approximately \$51.0 million. On December 31, 2013, we received aggregate funding of \$10.0 million from SVB, representing the full principal amount under the new loan agreement. Even after giving effect to the private placements and the new loan agreement, we will need to obtain additional funding in order to continue our operations and pursue our business plans. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We expect that our existing cash and cash equivalents will enable us to fund our operations and capital expenditure requirements for at least the next twelve months. Our future capital requirements will depend on many factors, including:

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our product candidates;

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

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

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

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

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

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

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

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

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

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing

Table of Contents

arrangements. Any or all of those sources of funding may not be available when needed on acceptable terms or at all. We do not have any committed external source of additional funds. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the ownership interest of existing equityholders will be diluted. For instance, our issuance of 9,010,238 shares of our common stock to investors in the November 2013 private placements equaled approximately 66.62% of our outstanding capital stock as of February 28, 2014, and has diluted the ownership interest of our other existing equityholders. Also, the terms of any additional equity securities that may be issued in the future may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing may not be available when needed and may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings or relationships with third parties when needed or on acceptable terms, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under applicable SEC rules.

Table of Contents

BUSINESS

Corporate Overview

General

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

On October 31, 2013, Ignyta effected a 100-to-one reverse stock split of its issued and outstanding shares of common stock, and all share information in this prospectus with respect to Ignyta gives retroactive effect to that reverse stock split.

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

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

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

Emerging Growth Company and Smaller Reporting Company Status

The Jumpstart Our Business Startups Act of 2012, or the JOBS Act, establishes a class of company called an emerging growth company, which generally is a company whose initial public offering was completed after December 8, 2011 and had total annual gross revenues of less than \$1 billion during its most recently completed fiscal year. Additionally, Section 12b-2 of the Securities Exchange Act of 1934, as amended, or the Exchange Act, establishes a class of company called a smaller reporting company, which generally is a company with a public float of less than \$75 million as of the last business day of its most recently completed second fiscal quarter or, if such public float is \$0, had annual revenues of less than \$50 million during the most recently completed fiscal year for which audited financial statements are available. We currently qualify as both an emerging growth company and a smaller reporting company.

As an emerging growth company and a smaller reporting company, we are eligible to take advantage of certain extended accounting standards and exemptions from various reporting requirements that are not available to public reporting companies that do not qualify for those classifications, including without limitation the following:

An emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. This

Table of Contents

allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected to avail ourselves of this extended transition period and, as a result, we will not be required to adopt new or revised accounting standards on the dates on which adoption of such standards is required for other public reporting companies.

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

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

Neither an emerging growth company nor a smaller reporting company is required to comply with the requirement of auditor attestation of internal controls over financial reporting, which is required for other public reporting companies by Section 404 of the Sarbanes-Oxley Act of 2002.

A company that is either an emerging growth company or a smaller reporting company is eligible for reduced disclosure obligations regarding executive compensation in its periodic and annual reports, including without limitation exemption from the requirement to provide a compensation discussion and analysis describing compensation practices and procedures.

A company that is either an emerging growth company or a smaller reporting company is eligible for reduced financial statement disclosure in registration statements, which must include two years of audited financial statements rather than the three years of audited financial statements that are required for other public reporting companies. Smaller reporting companies are also eligible to provide such reduced financial statement disclosure in annual reports on Form 10-K.

For as long as we continue to be an emerging growth company and/or a smaller reporting company, we expect that we will take advantage of the reduced disclosure obligations available to us as a result of those respective classifications. We will remain an emerging growth company until the earlier of (i) the last day of the fiscal year following the fifth anniversary of the date of the first sale of our common stock pursuant to an effective registration statement under the Securities Act, which was on February 15, 2013; (ii) the last day of the fiscal year in which we have total annual gross revenues of \$1 billion or more; (iii) the date on which we have issued more than \$1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under applicable SEC rules. We expect that we will remain an emerging growth company for the foreseeable future, but cannot retain our emerging growth company status indefinitely and will no longer qualify as an emerging growth company on or before December 31, 2018. We will remain a smaller reporting company until we have a public float of \$75 million or more as of the last business day of our most recently completed second fiscal quarter, and we could retain our smaller reporting company status indefinitely depending on the size of our public float.

Business Overview

We are a precision medicine biotechnology company dedicated to discovering or acquiring, then developing and commercializing, precisely targeted new drugs for cancer patients whose tumors harbor specific molecular alterations. We are pursuing an integrated drug and diagnostic, or Rx/Dx, strategy, where we anticipate pairing each of our product candidates with biomarker-based companion diagnostics, developed by us or by third parties with which we may partner, that are designed to identify the patients that are most likely to benefit from the use of the drugs we may develop. Our current development plans focus on two product candidates: RXDX-101, a tyrosine kinase inhibitor directed to the Trk family tyrosine kinase receptors (TrkA, TrkB and TrkC), ROS1 and

Table of Contents

ALK proteins, which is in a Phase I/II clinical study in molecularly defined patient populations for the treatment of solid tumors; and RXDX-102, a tyrosine kinase inhibitor directed to the Trk family tyrosine kinase receptors. As a result of the preliminary Phase I results relating to RXDX-101 that we have seen to date, we have decided to designate RXDX-102 as a back-up compound to RXDX-101. Accordingly, we will not devote further development resources to RXDX-102 unless the development program for RXDX-101 is unsuccessful.

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

We currently have no products that have obtained marketing approval in any jurisdiction. We have not generated revenues since inception and do not expect to do so in the foreseeable future due to the early stage nature of our current product candidates. We had net losses for the year ended December 31, 2013 of \$14.2 million, and we had an accumulated deficit as of December 31, 2013 of \$15.6 million.

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

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

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

proprietary tumor samples, as well as publicly available data from tens of thousands of tumor samples.

Table of Contents

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

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

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

Our ability to identify innovative cancer targets and develop drugs against them is enabled by, and dependent on, a set of essential capabilities and the experience of our drug discovery and management team. Key aspects of our core drug discovery capabilities include the ability to perform x-ray crystallography on protein targets, conduct *in silico* structure-based drug design and run virtual chemistry screens. Once compounds with activity against our target have been identified by those or other tests and procedures, our drug discovery and scientific team further pursues the drug development process. The members of our team have significant experience in medicinal chemistry, lead optimization, ADME & PK (the study of absorption, distribution, metabolism, excretion, and pharmacokinetics), preclinical development and clinical development, and have collectively led or contributed to the development of multiple drugs approved by the U.S. Food and Drug Administration, or the FDA, including several cancer therapeutics.

Cancer Background

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

Cancer is the second leading cause of death in the United States, exceeded only by heart disease. The American Cancer Society, or ACS, estimated that, in 2013, there would be approximately 1.6 million new cases of cancer and approximately 580,000 deaths from cancer in the United States. The World Health Organization estimated that 7.6 million people worldwide died of cancer in 2008. According to ACS data, lung, colon and rectal, breast and

prostate cancer are the most prevalent cancers in the United States.

Table of Contents

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

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

Targeted Therapies. The next approach to pharmacological cancer treatment was to develop drugs, referred to as targeted therapeutics, that target specific biological molecules in the human body that play a role in rapid cell growth and the spread of cancer. Targeted therapeutics are designed to preferentially kill cancer cells and spare normal cells, to improve efficacy and minimize side effects. The drugs are designed to attack either a target that causes uncontrolled growth of cancer cells because of either a specific genetic alteration primarily found in cancer cells but not in normal cells, or a target that cancer cells are more dependent on for their growth than normal cells. These drugs focus on eradicating processes that help the cancer cell survive, but not on the oncogenes, which are the drivers or cause of the cancer itself.

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

Strategy

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

Utilize public and proprietary sources of tumor samples and cancer data so that we are informed by a rich knowledge base. We have assembled a proprietary database of hundreds of tumor samples from

Table of Contents

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

Apply a multi-omics approach to discover activating molecular alterations that drive cancer biology. We believe that genetic insight can be very valuable in understanding cancer biology, but that the exploration of biological factors in addition to genetics can provide a more comprehensive understanding of the precise activating molecular alterations that drive oncogenicity. Thus, when we mine our Oncolome database to seek new cancer biomarkers and potential drug targets, we often explore epigenetic phenomena, such as DNA methylation patterns, in addition to DNA sequencing and transcript counting. Our team has identified potential cancer targets that are marked by epigenetic alterations that we may not have identified had we applied a genetic approach alone.

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

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

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

Test our product candidates only in the patients who we believe are most likely to derive benefit. We plan to use biomarkers both to identify the activating molecular alterations that represent the drug targets that we

wish to pursue, and to precisely define the patient populations in which we would test those product candidates based on the presence of the biomarkers associated with those specific alterations. If our product candidates demonstrate a therapeutic benefit in those specific molecularly defined patients, then, provided that we are able to complete appropriate clinical trials and obtain regulatory approvals for those product candidates, we intend to use biomarkers to inform physicians which patients are strong candidates to receive commercial access to the applicable drugs.

Table of Contents

Develop, or pursue relationships with third parties to develop, companion diagnostics to assist in identifying appropriate patients for any product candidates we are able to successfully commercialize. We believe that the availability of high quality companion diagnostics is essential to formalize biomarker discovery and utilization into a platform that can be used by regulators, physicians, payors and, most importantly, patients themselves, to facilitate administration of the applicable therapeutics to the most appropriate patients. A companion diagnostic is a test or measurement that evaluates the presence of biomarkers in a patient, which information can then assist physicians in selecting the specific drugs or treatments that may be most effective for that patient. With respect to our proposed and potential future product candidates, we believe that any high quality companion diagnostics that we or third parties are able to successfully develop could be used to select patients for late stage clinical testing, to inform regulators precisely which patients should be indicated for access to the therapeutics, to advise physicians and patients which individuals are good candidates for treatment with the therapeutics, and to guide payors as to the value the therapeutics provide to well-defined patients and the circumstances under which the therapeutics should be reimbursed.

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

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

Pipeline

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

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

RXDX-101: Lead Oncology Clinical Asset

RXDX-101 is a new chemical entity that we in-licensed from NMS. RXDX-101 is an orally available, selective tyrosine kinase inhibitor of the Trk family tyrosine kinase receptors (TrkA, TrkB and TrkC), ROS1 and

Table of Contents

ALK proteins. RXDX-101 is designed as a targeted therapeutic candidate to treat patients with cancers that harbor activating alterations to TrkA, TrkB, TrkC, ROS1 or ALK. Candidate alterations include gene rearrangements or mutations, splice variants, increased gene copy number and increased gene expression.

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

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

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

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

About ROS1. ROS1 belongs to the insulin-receptor superfamily. Like other tyrosine kinase receptor molecules, it plays a role in relaying growth signals from the environment outside the cell into the cell's nucleus. ROS1 is one of two orphan receptor tyrosine kinase family members with no known binding ligand. Genetic changes in ROS1, such as fusions, rearrangements, mutations or copy number increases, create oncogenes, which can lead to cancer. Molecular rearrangements of ROS1 create fusion proteins with constitutively active kinase domains that activate downstream signaling pathways, which lead to oncogenic properties in cells, including uncontrolled proliferation and resistance to cell death with increased tumor cell survival. ROS1 was first discovered in NSCLC patients in the form of a ROS fusion protein (six different partners for ROS1). Two other genetic rearrangements of ROS1 have been detected in a variety of other cancers, including glioblastoma multiforme, cholangiocarcinoma, ovarian cancer, gastric

adenocarcinoma, colorectal cancer, inflammatory myofibroblastic tumor, angiosarcoma and epitheloid hemangioendothelioma.

Table of Contents

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

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

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

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

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

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

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

The potential ability of RXDX-101 to act as a potent inhibitor of the TrkA, TrkB, TrkC, ROS1 and ALK proteins, as well as its observed ability to be administered orally and reach systemic circulation, known as oral bioavailability, and its observed ability to cross the blood brain barrier in preclinical studies, attracted us to the profile of this product candidate and support the market opportunity for the product.

RXDX-101 Preclinical Data

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

Table of Contents

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

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

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

Table of Contents

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

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

Phase I/II Clinical Trial

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

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

Secondary objectives of this trial are to:

determine the process by which RXDX-101 is distributed and metabolized in the body, which is referred to as pharmacokinetics;

Table of Contents

assess the biochemical and physiological effects of RXDX-101 on the human body, which is referred to as pharmacodynamics; and

evaluate any early evidence of anti-tumor activity in patients with TrkA-, ROS1- or ALK-positive tumors. The Phase I/II trial is not powered to show results with statistical significance. Statistical significance means that an effect is unlikely to have occurred by chance. Clinical trial results are considered statistically significant when the probability of the results occurring by chance, rather than from the efficacy of the product candidate, is sufficiently low. Since this trial is not powered to show results with statistical significance, the results from the trial may be attributable to chance and not the clinical efficacy of RXDX-101. This trial design is customary for a Phase I and some Phase II clinical trials, the principal purpose of which is to provide the basis for the design of larger, definitive trials that are powered by the addition of more patients to potentially show statistical significance. Pending guidance from regulatory agencies such as the FDA, we would likely design any later stage trials that are intended to support marketing approval applications to show statistical significance. We would do so by enrolling a larger number of patients based on the clinical data observed in earlier trials.

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

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

RXDX-101 Companion Diagnostic

Several companion diagnostic technologies are available for measuring alterations in TrkA, ROS1 and ALK. There is an FDA-approved fluorescence in situ hybridization, or FISH, test for measuring ALK translocations (Vysis, manufactured by Abbott Molecular). There is also a commercially available FISH test for measuring ROS1 fusion proteins, and we are aware of at least one group that has developed a FISH test for measuring TrkA fusion proteins. TrkA fusion proteins can also be measured by immunohistochemistry, or IHC, using commercially available antibodies. In addition, NMS has developed polymerase chain reaction, or PCR, assays for measuring fusion proteins for each of TrkA, TrkB, TrkC, ROS1 and ALK. Finally, several commercial, as well as academic, groups evaluate sequence mutations and translocations of TrkA, TrkB, TrkC, ROS1 and ALK by next generation sequencing. It is our intent to evaluate each of these candidate diagnostic approaches for measuring alterations to TrkA, TrkB, TrkC, ROS1 and ALK and select a technology to be pursued by us or a third-party collaborator, after taking into consideration scientific and commercial factors.

RXDX-102: Preclinical Asset

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

RXDX-102 Preclinical Data

RXDX-102 is an orally available selective inhibitor of TrkA, TrkB and TrkC. In *in vitro* studies performed to date, RXDX-102 achieves single digit nanomolar inhibition of TrkA, TrkB and TrkC enzymatic assays.

Table of Contents

RXDX-102 has been tested *in vivo* in four animal species to date, the mouse, rat, dog and primate. It has demonstrated *in vivo* antitumor activity against various TrkA-, TrkB- or TrkC-driven mouse xenograft models of cancer, and has also demonstrated oral bioavailability in all four species tested to date.

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

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

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

RXDX-102 Companion Diagnostic

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

Spark-1 through Spark-6

In our mining of our Oncolome database for molecular alterations that frequently occur in tumor tissue samples to date, we have identified six molecular targets, which, when altered, we believe to drive tumor growth. We refer to these six targets as Spark-1 through Spark-6. The six Spark targets consist of a combination of genetic and epigenetic targets. Although our research and development of these targets is in a very early stage, we believe that activation of these targets, via over-expression or gene rearrangement, may be oncogenic by

Table of Contents

promoting cell growth and survival in certain tissues. Additionally, though these protein targets are not yet validated, we believe that inhibition of the activated forms of these proteins in cancer-like cells may lead to impaired cell growth or cell death. We have prioritized three of these targets (Spark-1, Spark-2 and Spark-3) and have initiated target validation and small molecule drug discovery activities against some of these targets. Such discovery activities include, or may in the future include, but are not limited to: x-ray crystallography, structure-based drug design, virtual screening, *in vitro* screening, *in vivo* screening, medicinal chemistry and lead optimization. We intend to develop our first IND candidate against one of the Spark-1, Spark-2 or Spark-3 targets by as early as 2015.

License Agreement with NMS

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

Under the terms of the license agreement, on November 6, 2013, we issued to NMS a warrant to acquire up to 16,667 shares of our common stock, which has an exercise price of \$6.00 per share and is exercisable at any time at the option of the holder until November 6, 2018. The terms of the license agreement also provide for an up-front payment to NMS of \$7.0 million, and we made a cash payment to NMS for the full amount on November 14, 2013. When and if commercial sales of a product based on either or both of RXDX-101 or RXDX-102 begin, we will be obligated to pay NMS tiered royalties ranging from a mid-single digit percentage to a low double digit percentage (between 10% and 15%) of our net sales, depending on the amount of our net sales, with standard provisions for royalty offsets to the extent we obtain any rights from third parties to commercialize the product. We are also obligated under the terms of the license agreement to engage NMS to perform services valued at \$1.0 million or more between November 6, 2013 and December 31, 2014, which services could include, among others at our election, manufacture and supply services, technology transfer activities, preclinical activities, process development activities and assay development activities. The license agreement also requires that we make development and regulatory milestone payments to NMS of up to \$105.0 million in the aggregate if specified clinical study initiations and regulatory approvals are achieved across multiple products or indications. The first such milestone payment is not due until we elect to initiate the first randomized Phase II clinical trial, which, based on our current estimates and certain assumptions, we anticipate could occur as early as 2015.

The license agreement with NMS will remain in effect until the expiration of all of our royalty and sublicense revenue payment obligations to NMS. Those payment obligations commence after the first commercial sale of a product covered by the claims of any patent subject to the license agreement, and continue, on a product-by-product and country-by-country basis, through the longer of (i) the expiration of the last-to-expire valid patent in such country with claims covering such product or (ii) 10 years after the first commercial sale of such product in such country. The license agreement may be terminated under the following circumstances: (a) prior to the first commercial sale of a product covered by the agreement, if we provide NMS with 60 days' prior written notice of our termination of the agreement, (b) after the first commercial sale of any product covered by the agreement, if we provide NMS with three months' prior written notice of our termination.

Table of Contents

of the agreement (in which case NMS may then accelerate the effective date of the termination to not less than 30 days after our notice), or (c) upon a material breach by either party under the agreement, which breach is not cured within 30 days with respect to payment defaults or within 60 days with respect to any other breach (which cure period may be extended to up to 120 days for breaches other than payment defaults). As a result, if we fail to meet our payment or other obligations under the license agreement and are unable to cure any such failure within the specified cure periods, NMS could terminate the license agreement and we would lose our rights to RXDX-101 and RXDX-102.

Competition

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

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

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

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

The most common methods of treating patients with cancer are surgery, radiation and drug therapy, including chemotherapy, hormone therapy and targeted drug therapy or a combination of such methods. There are a variety of available drug therapies marketed for cancer. In many cases, these drugs are administered in combination to enhance efficacy. While our product candidates, if any are approved, may compete with these existing drug and other therapies, to the extent they are ultimately used in combination with or as an adjunct to these therapies, our product candidates may not be competitive with them. Some of the currently approved drug therapies are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well established therapies and are widely accepted by physicians, patients and third-party payors. As a result, obtaining market acceptance of, and a gaining significant share of the market for, any of our product candidates that we successfully

introduce to the market will pose challenges.

Table of Contents

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

RXDX-101

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

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

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

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

RXDX-102

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

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

Spark-1, Spark-2 and Spark-3

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

Commercialization

We have not yet established a sales, marketing or product distribution infrastructure because our lead candidates are still in discovery, preclinical or early clinical development. We anticipate that we will retain

Table of Contents

commercial rights in the United States for any of our product candidates for which we may in the future receive marketing approvals. We currently anticipate that, when appropriate, we will seek to access the United States oncology market through a focused, specialized, internal sales force.

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

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

We currently expect that any third parties with which we may collaborate in the future on the development of any commercial companion diagnostics for use with our therapeutic products will most likely hold the commercial rights to those diagnostic products. We expect that we would coordinate closely with any future diagnostic collaborators in connection with the marketing and sale of such diagnostic products and our related therapeutic products.

Manufacturing

We do not own or operate, and currently have no plans to establish, any manufacturing facilities. We currently rely, and expect to continue to rely, on third parties for the manufacture of our product candidates for preclinical and clinical testing, as well as for commercial manufacture of any products that we may commercialize. Our license agreement with NMS requires NMS to provide us with its existing inventory of clinical supply of RXDX-101, which can help support our planned expansion cohorts of the ongoing Phase I/II clinical trial of that product candidate. 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. For all of our product candidates, we plan to identify and qualify manufacturers to provide the active pharmaceutical ingredient and fill-and-finish services prior to submission of a new drug application, or NDA, to the FDA.

RXDX-101 and RXDX-102 are organic compounds of low molecular weight, generally called small molecules. We believe that they can be manufactured in reliable and reproducible synthetic processes from readily available materials. We believe that the chemistry is amenable to scale-up and does not require unusual or expensive equipment in the manufacturing process. We expect to continue to develop product candidates that can be produced cost-effectively at contract manufacturing facilities.

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

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our product candidates and our core technologies, including novel biomarker and

Table of Contents

diagnostic discoveries and other know-how, to operate without infringing any intellectual property rights of others and to prevent others from infringing our proprietary or intellectual property rights. We expect that we will seek to protect our proprietary and intellectual property position by, among other methods, licensing or filing our own U.S., international and foreign patent applications related to our proprietary technology, inventions and improvements that are important to the development and implementation of our business. We also rely on trade secrets, know-how and continuing technological innovation to develop and maintain our proprietary and intellectual property position, which we generally seek to protect through contractual obligations with third parties.

We currently, and expect that we will continue to, file or license patent applications directed to our key product candidates in an effort to establish intellectual property positions regarding new chemical entities relating to these product candidates, as well as uses of new chemical entities in the treatment of various cancers. We also intend to seek patent protection, if available, with respect to biomarkers that may be useful in selecting the right patient population for use of any of our product candidates. We own or exclusively license a patent portfolio consisting of two issued U.S. patents and their respective counterparts in a number of foreign jurisdictions, nine pending U.S. patent applications, three pending applications under the Patent Cooperation Treaty and corresponding pending patent applications in a number of foreign jurisdictions. The issued U.S. patents and patent applications covering RXDX-101 and RXDX-102 are as follows:

U.S. Patent No. 8,299,057 includes compound claims for RXDX-101, composition claims for RXDX-101 and claims to a method of manufacturing RXDX-101. This patent is expected to expire in 2029 (absent patent term extension) if all maintenance fees are timely paid. Related U.S. Application No. 13/611,679 claims methods of treatment using RXDX-101 and is allowed. The patent issuing from this application is expected to expire in 2028 if all maintenance fees are timely paid, absent patent term adjustment or extension. Related international patents have issued in New Zealand, South Africa and Ukraine, and related applications are pending in Europe (allowed pending validation), Argentina, Australia, Brazil, Canada, China (People's Republic), Hong Kong, India, Indonesia, Israel, Japan, Korea, Mexico, Philippines, Singapore, Taiwan and Thailand. All such international patents and applications contain substantially the same disclosure and support for the same types of claims as issued in U.S. Patent No. 8,299,057, although the actual claims will vary on a country-by-country basis. All issued international patents in this family are expected to expire in 2028 if all maintenance fees and annuities are timely paid.

U.S. Patent No. 8,114,865 includes compound claims for RXDX-102, composition claims for RXDX-102, claims for methods of treatment using RXDX-102 and claims to a method of manufacturing RXDX-102. This patent is expected to expire in 2028 (absent patent term extension) if all maintenance fees are timely paid. Related international patents have issued in Japan and Mexico, and related applications are pending in the European Patent Office (allowed pending validation), Australia, Brazil, Canada, the Eurasian Patent Organization and India. All such international patents and applications contain substantially the same disclosure and support for the same types of claims as issued in U.S. Patent No. 8,114,865, although the actual claims will vary on a country-by-country basis. All issued international patents in this family are expected to expire in 2027 if all maintenance fees and annuities are timely paid.

A provisional application claiming methods of synthesis of RXDX-102 has been filed. Any claims issuing from this application in the United States are expected to expire in 2034 (absent patent term adjustment or extension) if all maintenance fees are timely paid.

A provisional application claiming methods of using RXDX-101 and RXDX-102 in coordination with identifying ROS1 status has been filed. Any claims issuing from this application in the United States are expected to expire in 2034 (absent patent term adjustment or extension) if all maintenance fees are timely paid.

Table of Contents

PCT Application PCT/EP2013//060534 claiming methods of synthesis of RXDX-101 has been filed and is pending. Related applications have been filed in non PCT-signatories Argentina, Pakistan and Taiwan. This PCT application may later enter prosecution in the United States or in one or more of the over 140 PCT signatory countries or jurisdictions. Any claims issuing from such a U.S. or foreign application would be expected to expire in 2032 (absent patent term adjustment or extension) if all maintenance fees are timely paid.

Our other pending U.S. patent applications and a significant portion of our pending patent applications in foreign jurisdictions pertain to our DNA methylation biomarkers and our platform for generating DNA methylation biomarkers, as well as the use of such biomarkers to diagnose, prognose and select treatments for certain autoimmune diseases. We are not presently pursuing these activities as a material aspect of our business and operations. We would expect that any patents that may issue from these pending U.S. patent applications would likely expire between 2031 and 2033; however, any and all of these patent applications may not result in issued patents.

In addition to the patent applications that we have filed as of the date of this prospectus, we intend to file additional applications covering potential discoveries that we may make in relation to our drug discovery and biomarker activities directed to the Spark-1 through Spark-6 targets. We plan to continue to expand our intellectual property portfolio by filing patent applications directed to dosage forms, methods of treatment and additional inhibitor compounds of oncology molecular targets and their derivatives. Specifically, we anticipate that we will seek patent protection in the United States and internationally for novel compositions of matter covering the compounds, the chemistries and processes for manufacturing these compounds, the use of these compounds in a variety of therapies and the use of biomarkers for patient selection for these compounds. Of course, these or other patent applications that we may file or license from third parties may not issue as patents, and any issued patents may have claims that are substantially more limited than the patents' disclosure. Any issued claims may be of a scope that may reduce their value and/or may be challenged, invalidated or circumvented. See Risk Factors Rights Related to Our Intellectual Property.

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

With respect to our proprietary DNA methylation analysis platform, we consider trade secrets and know-how to be a critical component of our intellectual property. Trade secrets and know-how can be difficult to protect. In particular, with respect to this technology platform we anticipate that these trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles describing the methodology and the movement of personnel skilled in the art from academic to industry scientific positions. As a result, those proprietary trade secrets and know-how may lose their value to us over a period of time, and we may lose any competitive advantage afforded by them as they become public knowledge.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries, extensively regulate, among other things, the research, development, testing, manufacture, including any manufacturing changes, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution,

Table of Contents

marketing, post-approval monitoring and reporting, import and export of pharmaceutical products, such as those we are developing.

United States Drug Approval Process

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

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

completion of preclinical laboratory tests, animal studies and formulation studies in compliance with GLP regulations;

submission to the FDA of an IND, which must become effective before human clinical trials may begin;

approval of each phase of the proposed clinical trials and related informed consents by an institutional review board, or IRB, at each clinical site where such trial will be performed;

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

submission to the FDA of an NDA;

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

FDA review and approval of the NDA.

Preclinical Studies and IND

Preclinical studies include laboratory evaluation of product chemistry and formulation, as well as *in vitro* and animal studies to assess the potential for adverse events and, in some cases, to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations for safety/toxicology studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing

information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, to the FDA as part of an IND. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Table of Contents

Clinical Trials

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

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

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

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

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

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and, more frequently, if serious adverse events occur. The FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the preclinical studies and clinical trials, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most NDAs is subject to a substantial application user fee.

The FDA generally conducts a preliminary review of all NDAs to determine whether they are sufficiently complete to permit substantive review within the first 60 days after submission before accepting them for filing. The FDA may request additional information in connection with this preliminary review rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is subject to further review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified

Table of Contents

performance goals in the review of NDAs. Under these goals, the FDA has committed to review most such applications for non-priority products within 10 months, and most applications for priority review products, that is, drugs that the FDA determines represent a significant improvement over existing therapy, within six months. The FDA may also refer applications for novel drugs or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. The FDA is not required to adhere its review time goals, and its review could experience delays that cause those goals to not be met.

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

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

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

Post-Market Drug Regulation

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

In addition, drug manufacturers with which we partner and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and

Table of Contents

are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMPs requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMPs and impose reporting and documentation requirements upon drug developers and their manufacturers. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality control to maintain cGMPs compliance.

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

restrictions on the marketing or manufacturing of the product, 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; or

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

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

Programs for Expedited Review and Approval

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

Fast Track Designation. The FDA is required to facilitate the development and expedite the review of drugs that are intended for the treatment of a serious or life-threatening condition for which there is no effective treatment and that demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor

of a new product candidate may request the FDA to designate the product for a specific indication as a fast track product concurrent with or after the submission of the IND for the product candidate. The FDA must determine if the product candidate qualifies for fast track designation within 60 days after receipt of the sponsor's request.

In addition to other benefits, such as the ability to use surrogate endpoints (see the description of surrogate endpoints under Accelerated Approval below) and have greater interactions with the FDA, the FDA may

Table of Contents

initiate review of sections of a fast track product's NDA before the application is complete. This rolling review is available if the applicant provides and the FDA approves a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's review time goal for a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

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

Accelerated Approval. Under the FDA's accelerated approval regulations, the FDA may approve a drug for a serious or life-threatening illness that provides meaningful therapeutic benefit to patients over existing treatments based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. In clinical trials, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or sooner than clinical endpoints. A product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase IV or post-approval clinical trials to validate the surrogate endpoint or otherwise confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Breakthrough Therapy Designation. Under the provisions of the new Food and Drug Administration Safety and Innovation Act enacted in 2012, a sponsor can request designation of a product candidate as a breakthrough therapy. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Alternative Approval Pathways

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

Orphan Drugs. Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally defined as a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the

regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-

Table of Contents

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

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

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

the required patent information has not been filed;

the listed patent has expired;

the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or

the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicate that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration

of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA also will not be approved until any applicable non-patent exclusivity period, such as exclusivity for obtaining approval of a new chemical entity, for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active part of any molecule (moiety) during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years

Table of Contents

following the original product approval. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an ANDA if a listed drug contains a previously approved active moiety, but FDA requires as a condition of approval new clinical trials conducted by or for the sponsor. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication. Under the Best Pharmaceuticals for Children Act, federal law also provides that periods of patent and non-patent marketing exclusivity listed in the Orange Book for a drug may be extended by six months if the NDA sponsor conducts pediatric studies identified by the FDA in a written request. If such a written request is issued by the FDA, the FDA must grant pediatric exclusivity no later than six months prior to the date of expiration of patent or non-patent exclusivity in order for the six-month pediatric extension to apply to that exclusivity period.

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

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

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

Combination Products

The FDA regulates combinations of products that cross FDA centers, such as drug, biologic or medical device components that are physically, chemically or otherwise combined into a single entity, as a combination product. The FDA center with primary jurisdiction for the combination product will take the lead in the premarket review of the product, with the other center consulting or collaborating with the lead center.

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

Often it is difficult for the OCP to determine with reasonable certainty the most important therapeutic action of the combination product. In those difficult cases, the OCP will consider consistency with other combination

Table of Contents

products raising similar types of safety and effectiveness questions, or which center has the most expertise to evaluate the most significant safety and effectiveness questions raised by the combination product.

A sponsor may use a voluntary formal process, known as a Request for Designation, when the product classification is unclear or in dispute, to obtain a binding decision as to which center will regulate the combination product. If the sponsor objects to that decision, it may request that the agency reconsider the decision.

FDA Regulation of Companion Diagnostics

We may seek to develop, or seek to partner with third parties to develop *in vitro* and *in vivo* companion diagnostics for use in selecting the patients that we believe will respond to our drug therapeutics.

FDA officials have issued draft guidance that, when finalized, would address issues critical to developing *in vitro* companion diagnostics, such as biomarker qualification, establishing clinical validity, the use of retrospective data, the appropriate patient population and when the FDA will require that the device and the drug be approved simultaneously. The draft guidance issued in July 2011 states that if safe and effective use of a therapeutic product depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic product. The FDA has yet to issue further guidance regarding these matters, and it is unclear whether it will do so or what the scope of any additional guidance would be.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to a cancer treatment to obtain pre-market approval, or PMA, simultaneously with approval of the drug.

Medical Device Approval Pathways

A medical device, including an *in vitro* diagnostic, or IVD, to be commercially distributed in the United States must receive either 510(k) clearance or PMA approval from the FDA prior to marketing. There are three classes of medical devices recognized by the FDA, Class I (the least regulated), Class II, and Class III (the most regulated), and devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life supporting or implantable devices, or devices deemed not substantially equivalent to a previously 510(k) cleared device or a pre-amendment Class III device for which PMA applications have not been called, are placed in Class III requiring PMA approval. The PMA approval pathway requires proof of the safety and effectiveness of the device to the FDA's satisfaction.

A PMA for an IVD must provide extensive preclinical and clinical trial data. Preclinical data for an IVD includes many different tests, including how reproducible the results are when the same sample is tested multiple times by multiple users at multiple laboratories. The clinical data need to establish that the test is sufficiently safe, effective and reliable in the intended use population. In addition, the FDA must be convinced that a device has clinical utility, meaning that an IVD provides information that is clinically meaningful. A biomarker's clinical significance may be obvious, or the applicant may be able to rely upon published literature or submit data to the FDA to show clinical utility.

A PMA also must provide information about the device and its components regarding, among other things, device design, manufacturing and labeling. The sponsor must pay an application fee to the FDA upon submission of a PMA.

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

Table of Contents

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

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

If the FDA's evaluation of the PMA is favorable, the FDA typically issues an approvable letter requiring the applicant's agreement to specific conditions, such as changes in labeling, or specific additional information, such as submission of final labeling, in order to secure final approval of the PMA. If the FDA concludes that the applicable criteria have been met, the FDA will issue a PMA for the approved indications, which can be more limited than those originally sought by the applicant. The PMA can include post-approval conditions that the FDA believes necessary to ensure the safety and effectiveness of the device, including, among other things, restrictions on labeling, promotion, sale and distribution. Failure to comply with the conditions of approval can result in an enforcement action, including the loss or withdrawal of the approval.

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

Clinical Trials and IDEs

A clinical trial is almost always required to support a PMA application. In some cases, one or more smaller Investigational Device Exemption, IDE, studies may precede a pivotal clinical trial intended to demonstrate the safety and efficacy of the investigational device.

All clinical studies of investigational devices must be conducted in compliance with the FDA's requirements. If an investigational device could pose a significant risk to patients pursuant to FDA regulations, the FDA must approve an IDE application prior to initiation of investigational use. IVD trials usually do not require an IDE, as the FDA does not judge them to be a significant risk because the results do not affect the patients in the study. However, for a trial where the IVD result directs the therapeutic care of patients with cancer, we believe that the FDA may consider the investigation to present significant risk and require an IDE application.

An IDE application must be supported by appropriate data, such as laboratory test results, showing that it is safe to test the device in humans and that the testing protocol is scientifically sound. The FDA typically grants IDE approval for a specified number of patients. A non-significant risk device does not require FDA approval of an IDE. Both significant risk and non-significant risk investigational devices require approval from IRBs at the study centers where the device will be used.

During the critical trial, the sponsor must comply with the FDA's IDE requirements for investigator selection, trial monitoring, reporting and record keeping. The investigators must obtain patient informed consent, rigorously follow

the investigational plan and study protocol, control the disposition of investigational devices and comply with all reporting and record keeping requirements. Prior to granting PMA approval, the FDA

Table of Contents

typically inspects the records relating to the conduct of the study and the clinical data supporting the PMA application for compliance with applicable requirements.

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

Post-Market Device Regulation

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

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

Foreign Regulation

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

The EMA grants orphan drug designation to promote the development of products that may offer therapeutic benefits for life-threatening or chronically debilitating conditions affecting not more than five in 10,000 people in the European Union. In addition, orphan drug designation can be granted if the drug is intended for a life threatening, seriously debilitating or serious and chronic condition in the European Union and without incentives it is unlikely that sales of the drug in the European Union would be sufficient to justify developing the drug. Orphan drug designation is only available if there is no other satisfactory method approved in the European Union of diagnosing, preventing or

treating the condition, or if such a method exists, the proposed orphan drug will be of significant benefit to patients. Orphan drug designation provides opportunities for free protocol

Table of Contents

assistance, fee reductions for access to the centralized regulatory procedures before and during the first year after marketing authorization and between 6 and 10 years of market exclusivity following drug approval.

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

In the European Union, new chemical entities qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from assessing a generic (abbreviated) application for eight years, after which generic marketing authorization can be submitted but not approved for two years. Even if a compound is considered to be a new chemical entity and the sponsor is able to gain the prescribed period of data exclusivity, another company nevertheless could also market another version of the drug if such company can complete a full MAA with a complete human clinical trial database and obtain marketing approval of its product.

Additional Regulations and Environmental Matters

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

The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Violations of the federal anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from participation in federal healthcare programs.

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

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

Additionally, the Prescription Drug Marketing Act, or the PDMA, imposes requirements and limitations upon the provision of drug samples to physicians, as well as prohibits states from licensing distributors of

Table of Contents

prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage, handling and record keeping. In addition, the PDMA sets forth civil and criminal penalties for violations. If we obtain approval from the FDA to market any of our drug product candidate, these product sampling restrictions may impact and curtail our marketing efforts to physicians.

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

In addition to regulatory schemes that apply, or may in the future apply, to our business, we are or may become subject to various environmental, health and safety laws and regulations governing, among other things, laboratory procedures and any use and disposal by us of hazardous or potentially hazardous substances in connection with our research and development activities. We do not presently expect such environmental, health and safety laws or regulations to materially impact our present or planned future activities.

Our Scientific Advisors

We have assembled a scientific advisory board that includes renowned experts in oncology, autoimmune disease, epigenetics, drug discovery and translational medicine. These advisors work in close collaboration with our scientific and drug discovery team to identify new research directions and accelerate our target validation and drug discovery programs.

Name

Garrett Brodeur, M.D.
Sai-Hong Ignatius Ou, M.D., Ph.D.
Daniel D. Von Hoff, M.D., F.A.C.P.
Gary Firestein, M.D.
Wei Wang, Ph.D.

Primary Affiliation

Children's Hospital of Philadelphia
University of California, Irvine
Translational Genomics Research Institute
University of California, San Diego
University of California, San Diego

Employees

As of February 28, 2014, we had 17 employees, 15 of whom were full-time, including 10 employees with M.D. or Ph.D. degrees, and two part-time employees. Of these full-time and part-time employees, 12 employees were engaged in research and development activities. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Facilities

We occupy approximately 3,945 rentable square feet of office and laboratory space in San Diego, California under a lease that expires in August 2016 and provides for monthly rent payments of approximately \$7,350, which amount will increase beginning in March 2014 to approximately \$9,941 per month and by additional amounts in the years thereafter, and an additional 1,841 rentable square feet of laboratory space in San Diego,

Table of Contents

California under a lease that expires in November 2014 and provides for monthly rent payments of approximately \$3,774. We believe that our facilities are sufficient to meet our current needs and that suitable additional space will be available as and when needed.

Legal Proceedings

Neither we nor our subsidiary is currently a party to, nor is our property the subject of, any material legal proceedings.

Table of Contents**MANAGEMENT AND CERTAIN CORPORATE GOVERNANCE MATTERS****Directors, Executive Officers and Certain Other Non-Executive Officers**

The table below sets forth the name, age and position of each of our directors and executive officers and certain other non-executive officer members of our scientific and drug development team as of February 28, 2014.

Name	Age	Position
<i>Directors and Executive Officers:</i>		
Jonathan E. Lim, M.D.	42	President, Chief Executive Officer and Chairman of the Board
Zachary Hornby	35	Chief Financial Officer, and Vice President, Corporate Development
Sara Zaknoen, M.D.	55	Chief Medical Officer
Matthew W. Onaitis	43	General Counsel and Secretary
James Bristol, Ph.D. ⁽¹⁾⁽³⁾	67	Director
Alexander Casdin ⁽¹⁾⁽²⁾⁽³⁾	46	Director
Heinrich Dreismann, Ph.D. ⁽¹⁾⁽²⁾	60	Director
James Freddo, M.D. ⁽²⁾⁽³⁾	59	Director
<i>Non-Executive Officer Management Team:</i>		
Jean-Michel Vernier, Ph.D.	52	Vice President, Medicinal Chemistry
Paul Pearson, Ph.D.	53	Consulting Vice President of PK, Drug Metabolism & Safety
Dave Matthews, Ph.D.	71	Consulting Vice President, Crystallography
Robert Shoemaker, Ph.D.	32	Senior Director of Bioinformatics

(1) Member of the compensation committee

(2) Member of the audit committee

(3) Member of the nominating and corporate governance committee

Business Experience

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

Jonathan E. Lim, M.D. Dr. Lim is a co-founder of Ignyta Operating and joined that company as Chairman, President and Chief Executive Officer at its inception in August 2011, and has continued in those roles with Ignyta since the closing of the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary. Prior to joining Ignyta Operating, Dr. Lim most recently served as Chairman and Chief Executive Officer of Eclipse Therapeutics, Inc., a private biotechnology company discovering and developing monoclonal antibody therapeutics targeting cancer stem cells, that he co-founded in March 2011 as a spinout from Biogen Idec and that was sold to

Bionomics Ltd., an Australian public biotechnology company discovering and developing drugs targeting oncology and central nervous system disorders, in September 2012. Dr. Lim currently serves as a member of the Board of Directors of Bionomics Ltd. Prior to founding Eclipse Therapeutics, Dr. Lim served as the President, Chief Executive Officer and a Director of Halozyme Therapeutics, Inc., a public biotechnology company, from May 2003 to December 2010. Prior to that, Dr. Lim's experience included management consulting at McKinsey & Company, a National Institutes of Health Postdoctoral Fellowship at Harvard Medical School and two years of general surgery residency at New York Hospital-Cornell. Dr. Lim has B.S. and M.S. degrees from Stanford, an M.D. from McGill University and an M.P.H. from Harvard University. We believe that Dr. Lim adds value to our Board of Directors based on his intimate knowledge of our business

Table of Contents

plans and strategies as a co-founder of our business and his extensive experience as an executive officer and director of multiple public and private biotechnology companies.

Zachary Hornby. Mr. Hornby joined Ignyta Operating in August 2012 as Vice President, Corporate Development and was appointed as its Chief Financial Officer in August 2013, and has continued in those roles with Ignyta since the closing of the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary. Prior to joining Ignyta Operating, Mr. Hornby served as senior director of business development at Fate Therapeutics, a public biopharmaceutical stem cell discovery and development company, from August 2010 to August 2012. Prior to Fate Therapeutics, Mr. Hornby was director of business development at Halozyme Therapeutics, a public biotechnology company, from January 2008 to August 2010. Prior to Halozyme Therapeutics, Mr. Hornby was senior product manager at Neurocrine Biosciences, a public biopharmaceutical company, from June 2006 to January 2008. Prior to Neurocrine Biosciences, Mr. Hornby served as a life sciences consultant at L.E.K. Consulting and in regulatory affairs and business development roles at Transkaryotic Therapies (acquired by Shire Pharmaceuticals in 2005), an orphan drug discovery and development company. Mr. Hornby is a director of Independa, Inc. Mr. Hornby holds B.S. and M.S. degrees in biology from Stanford University and an M.B.A. from Harvard Business School.

Sara Zaknoen, M.D. Dr. Zaknoen joined Ignyta on February 19, 2014. Prior to joining Ignyta, Dr. Zaknoen was Chief Medical Officer of Polynoma LLC from May 2012 to January 2014. From January 2007 until February 2012, Dr. Zaknoen served as the Chief Medical Officer of Tragara Pharmaceuticals, Inc. Prior to Tragara, Dr. Zaknoen was the Chief Medical Officer of Cabrellis Pharmaceuticals Corporation from September 2006 to December 2006, contributing to the sale of Cabrellis to Pharmion Corporation in November 2006. Dr. Zaknoen served as Executive Director of Phase 2/3 Clinical Oncology Research of Novartis Pharmaceuticals Corp. from September 2002 to September 2006, and she served as Director of Clinical Oncology Research of Schering-Plough Research Institute from April 1998 to September 2002. Dr. Zaknoen's prior positions also include Assistant Professor of Medicine at the University of Cincinnati Medical Center; Director of Experimental Therapeutics at the Western Pennsylvania Hospital, Western Pennsylvania Cancer Institute; Medical Staff Fellow at the National Cancer Institute; and internship, residency and fellowship in hematology/oncology at the University of Minnesota. Dr. Zaknoen holds a B.S. in Chemistry and Biology from Valparaiso University and an M.D. degree from the Indiana University School of Medicine.

Matthew W. Onaitis. Mr. Onaitis joined Ignyta on February 3, 2014. Prior to joining Ignyta, Mr. Onaitis was General Counsel of Trius Therapeutics, Inc. from May 2013 through its acquisition by Cubist Pharmaceuticals, Inc. in September 2013. Mr. Onaitis remained with Cubist assisting with the integration through December 2013. Mr. Onaitis was Senior Vice President, General Counsel and Secretary at Somaxon Pharmaceuticals, Inc. from May 2006 through Somaxon's acquisition by Pernix Therapeutics Holdings, Inc. in March 2013. Prior to Somaxon, Mr. Onaitis served as Associate General Counsel at Biogen Idec Inc., as Director, Legal Affairs at Elan Corporation plc, and in private practice specializing in corporate and commercial law. Mr. Onaitis is a director of SNP Bio, Inc. Mr. Onaitis holds a J.D. from Stanford Law School and a B.S. in mechanical engineering from Carnegie Mellon University.

James Bristol, Ph.D. Dr. Bristol joined the Board of Directors of Ignyta on February 28, 2014. Dr. Bristol worked for 33 years in drug discovery research and pre-clinical development at Schering-Plough, Parke-Davis and Pfizer, serving in various senior research and development roles. From 2003 until his retirement in 2007, Dr. Bristol was Senior Vice President of Worldwide Drug Discovery Research at Pfizer Global Research & Development. Dr. Bristol has been a Co-Chairman of the Board of Managers at Deciphera Pharmaceuticals, LLC since 2007 and serves as a Member of the Managing Board. He has also served as a Director of Mnemosyne Pharmaceuticals, Inc. since 2011. In 2009, Dr. Bristol joined Frazier Healthcare Ventures as a Senior Advisor. Dr. Bristol is the author of over 100 publications, abstracts and patents. He conducted postdoctoral research at the University of Michigan (N.I.H. Postdoctoral Fellow) and at The Squibb Institute for Medical Research. Dr. Bristol holds a Ph.D. in organic chemistry from the University

of New Hampshire and a B.S. in Chemistry from Bates College. We believe that Dr. Bristol adds value to our Board of Directors based on his experience in

Table of Contents

the biopharmaceutical industry including in management and as a director, as well as his expertise in drug discovery and development.

Alexander Casdin. Mr. Casdin joined the Board of Directors of Ignyta upon the closing of the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary. Alex Casdin is a private investor focused on the healthcare sector. From October 2011 through September 2012, Mr. Casdin was the Chief Financial Officer of Sophiris Bio, Corp., a Canadian public urology company. Prior to Sophiris Bio, Mr. Casdin served as the Vice President, Finance of Amylin Pharmaceuticals, a biopharmaceutical company that was acquired by Bristol-Myers Squibb in 2012, a position he held from October 2009 to October 2011. Prior to his position at Amylin Pharmaceuticals, Mr. Casdin founded and operated Casdin Advisors LLC, where he served as a strategic advisor to companies in the life sciences industry. Before founding Casdin Advisors, Mr. Casdin was the Chief Executive Officer and Portfolio Manager of Cooper Hill Partners, LLC, a healthcare investment fund. Mr. Casdin has also held previous positions at Pequot Capital Management and Dreyfus Corporation. Mr. Casdin currently serves on the board of directors of DiaVacs, a private clinical-stage biotechnology company focused on a treatment for Type 1 Diabetes, and as a member of the advisory boards of the Hassenfeld Center For Cancer & Blood Disorders and the Social Enterprise Program of the Columbia Business School, each of which are non-profit entities, and served on the board of directors of DUSA Pharmaceuticals, a specialty pharmaceutical company in the field of dermatology that was previously listed on the NASDAQ Stock Market and was acquired by Sun Pharmaceutical Industries Limited in December 2012, from January 2009 until December 2012. Mr. Casdin earned his B.A. degree from Brown University and his M.B.A., Beta Gamma Sigma, from Columbia Business School. We believe that Mr. Casdin adds value to our Board of Directors based on his experience with the financing and other aspects of company-building for enterprises in our industry.

Heinrich Dreismann, Ph.D. Dr. Dreismann joined the Board of Directors of Ignyta upon the closing of the October 31, 2013 merger in which Ignyta Operating became our wholly owned subsidiary. Dr. Dreismann currently serves on the boards of directors of several public and private diagnostic companies, including Myriad Genetics, Inc., a public molecular diagnostic company, GeneNews, a Canadian public molecular diagnostics company, and Med BioGene, Inc., a Canadian public life sciences company focused on genomic-based clinical laboratory diagnostic tests. Dr. Dreismann also served on the board of directors of Shrink Nanotechnologies, Inc., a nanotechnology company, from June 2009 until November 2011. Dr. Dreismann completed a career at Roche Molecular Systems in 2006, where he served since 1985 and held several senior positions, including President and Chief Executive Officer of Roche Molecular Systems, Head of Global Business Development at Roche Diagnostics and Member of Roche's Global Diagnostic Executive Committee. Dr. Dreismann earned a Master of Science in biology and a Doctor of Philosophy in microbiology/molecular biology from Westfaelische Wilhelms University in Muenster, Germany. He conducted his Post-Doctoral studies in microbial genetics at the Centre d'Etudes Nucleaires de Saclay, France. We believe that Dr. Dreismann adds value to our Board of Directors based on his experience as a member of boards of directors and senior management of public companies and his expertise in the molecular diagnostics field.

James Freddo, M.D. Dr. Freddo joined the Board of Directors of Ignyta on February 28, 2014. Previously Dr. Freddo was a consultant to Ignyta Operating from July 2013 to February 2014 holding the position of Chief Medical Officer. Prior to joining Ignyta Operating, he served as a consultant from April 2012 until May 2012 and as the Executive Vice President, Clinical Development and Chief Medical Officer from June 2012 until May 2013, in each case for Ruga Corporation, a private oncology biopharmaceutical company. Prior to that, he was the Chief Medical Officer and Senior Vice President, Drug Development at Anadys Pharmaceuticals, a drug development company focused on small molecule therapeutics that was previously listed on the NASDAQ Stock Market and was acquired by Roche in 2011, from July 2006 until March 2012, where he also served as a member of the Board of Directors from January 2011 until November 2011. Prior to joining Anadys Pharmaceuticals, Dr. Freddo served at Pfizer, a global research-based pharmaceutical company, in La Jolla, California from June 2002 until July 2006, holding the positions of Vice

President, Clinical Site Head and Development Site Head and, prior to that, Executive Director and leader of Oncology Clinical Development. Prior to joining Pfizer, Dr. Freddo held a variety of senior management positions at Wyeth-Ayerst Research from 1996 to 2002, in the

Table of Contents

Oncology, Infectious Diseases and Transplantation Immunology therapeutic areas. He has also served as a member of the Board of Directors for InfuSystems, Inc., a public healthcare products and services company, from 2008 until 2011. Dr. Freddo received an M.D. degree from the University of North Carolina, Chapel Hill, completed his residency training at University of California, San Diego and returned to Chapel Hill for his fellowship training in gynecologic oncology. We believe that Dr. Freddo adds value to our Board of Directors based on his experience as a member of boards of directors and senior management of life sciences companies and his expertise in drug development, clinical investigations and other aspects of our industry.

The following is a brief account of the education and business experience of the current non-executive officer members of our scientific and drug development team, who hold their respective positions with Ignyta Operating:

Jean-Michel Vernier, Ph.D. Dr. Vernier joined Ignyta Operating in June 2013 as Vice President, Medicinal Chemistry, after Ignyta Operating acquired Actagene, a discovery stage precision medicine company for which he was serving as a consultant holding the position of Vice President, Chemistry at the time of the acquisition. Prior to joining Actagene, Dr. Vernier served as Head of Chemistry of Ruga Corporation, a private oncology biopharmaceutical company, from February 2012 until April 2013. Prior to Ruga, Dr. Vernier was a Co-Founder and Vice President of Chemistry at Selexagen Therapeutics, a private cancer therapeutics company, from October 2010 until January 2012. Prior to co-founding Selexagen Therapeutics, Dr. Vernier served as Vice President of Discovery Chemistry at Ardea Biosciences, a private biotechnology small-molecule therapeutics company, from 2007 until 2010. Dr. Vernier has also led chemistry at Valeant Pharmaceuticals, Merck Research Laboratories and SIBIA Neurosciences. Dr. Vernier received a Ph.D. in synthetic organic chemistry from the University Louis Pasteur, Strasbourg, France and was a postdoctoral fellow at Colorado State University.

Paul Pearson, Ph.D. Dr. Pearson joined Ignyta Operating in July 2013 as a consultant holding the position of Vice President of Pharmacokinetics, Drug Metabolism & Safety, after Ignyta Operating acquired Actagene, a discovery stage precision medicine company for which he was serving as a consultant holding the position of Vice President of Pharmacokinetics, Drug Metabolism & Safety at the time of the acquisition. Dr. Pearson also currently serves as the President of Pearson Pharma Partners, a private drug development consulting company, and has served in such position since May 2008. Prior to joining Actagene, Dr. Pearson served as a consultant from August 2010 until June 2012 and as the Vice President, Preclinical Development from July 2012 until March 2013, in each case for Ruga Corporation, a private oncology biopharmaceutical company. Prior to that, Dr. Pearson served as Global Head and Vice President, Pharmacokinetics and Drug Metabolism (PKDM) at Amgen, Inc., a public biotechnology company focused on developing human therapeutics, from October 2003 to April 2008. Prior to Amgen, Dr. Pearson was Executive Director of Preclinical Drug Metabolism at Merck Research Laboratories, a global healthcare therapeutics company, from January 1998 until September 2003. Prior to Merck, Dr. Pearson held positions of increasing importance in drug metabolism at the Upjohn Company, a pharmaceutical manufacturing company. Dr. Pearson is the Editor of the Handbook of Drug Metabolism (2009).

Dave Matthews, Ph.D. Dr. Matthew joined Ignyta Operating in June 2013 as a consultant holding the position of Vice President of Crystallography, after Ignyta Operating acquired Actagene, a discovery stage precision medicine company for which he was serving as a consultant holding the position of Vice President of Crystallography at the time of the acquisition. Dr. Matthews is also currently Chairman of the Scientific Advisory Board for a broad-based consortium of partners participating in the Bill and Melinda Gates Foundation-funded initiative for Structure Guided Drug Discovery for Tuberculosis and Malaria. Prior to joining Actagene, Dr. Matthews served as a consultant for Ruga Corporation, a private oncology biopharmaceutical company, from May 2012 until November 2012. Prior to that, Dr. Matthews was a scientific founder of Selexagen Therapeutics, Inc., a private cancer therapeutics company, in March 2008. Prior to Selexagen Therapeutics, Dr. Matthews served on the Medicines for Malaria Ventures Expert Scientific Advisory Committee from November 2005 to November 2010. Prior to that, Dr. Matthews was

Distinguished Research Fellow, Head of Structural Biology, Computational Chemistry, and Bioinformatics at Pfizer, a global research-based pharmaceutical company, from Pfizer's acquisition of Warner Lambert and Agouron Pharmaceuticals in 2000 until 2005. Prior to that,

Table of Contents

Dr. Matthews was the scientific founder of Agouron Pharmaceuticals in 1985. Prior to Agouron Pharmaceuticals, Dr. Matthews was a postdoctoral fellow and later a faculty member in the Department of Chemistry at the University of California, San Diego from 1971 until 1985. Dr. Matthews received his Ph.D. in physical chemistry from the University of Illinois, Urbana-Champaign.

Robert Shoemaker, Ph.D. Dr. Shoemaker joined Ignyta Operating in January 2012 as Director of Bioinformatics and was appointed as Senior Director of Bioinformatics in January 2013. Prior to joining Ignyta Operating, Dr. Shoemaker was a Scientist at Illumina, Inc., a public life science company focused on the analysis of genetic variation and function, from March 2011 to January 2012. Prior to Illumina, Dr. Shoemaker was a Graduate Student and Postdoctoral Researcher at the University of California, San Diego from 2005 until 2011. Dr. Shoemaker has a Ph.D. and M.S. in chemistry, B.S. in biochemistry, and B.A. in German literature from the University of California, San Diego.

Term of Office of Directors

Our directors are elected at each annual meeting of stockholders and serve until the next annual meeting of stockholders or until their successor has been duly elected and qualified, or until their earlier death, resignation or removal.

Director Independence

Our Board of Directors has determined that Dr. Bristol, Mr. Casdin, Dr. Dreismann and Dr. Freddo are independent directors in accordance with the listing requirements of the NASDAQ Capital Market. The NASDAQ independence definition includes a series of objective tests, including that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by NASDAQ rules, our Board of Directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our Board of Directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our Board of Directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Involvement in Certain Legal Proceedings

None of our directors, executive officers, significant employees, promoters or control persons has been involved in any legal proceeding in the past 10 years that would require disclosure under Item 401(f) of Regulation S-K promulgated under the Securities Act.

Committees of the Board of Directors

Our board has established three standing committees—audit, compensation, and nominating and corporate governance each of which operates under a charter that has been approved by our board.

Our board has determined that all of the members of each of the board's three standing committees are independent as defined under the rules of the NASDAQ Capital Market. In addition, all members of the audit committee meet the independence requirements contemplated by Rule 10A-3 under the Exchange Act.

Table of Contents

Audit Committee

The audit committee's main function is to oversee our accounting and financial reporting processes and the audits of our financial statements. This committee's responsibilities include, among other things:

appointing our independent registered public accounting firm;

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

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

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