

Ignyta, Inc.
Form 424B5
June 09, 2015
Table of Contents

Filed pursuant to Rule 424(b)(5)
Registration No. 333-202403

This prospectus supplement relates to an effective registration statement under the Securities Act of 1933, but is not complete and may be changed. This prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED JUNE 9, 2015

PROSPECTUS SUPPLEMENT

To Prospectus Dated March 13, 2015

\$75,000,000

Common Stock

We are offering _____ shares of our common stock as described in this prospectus supplement and the accompanying prospectus.

Our common stock is listed on the Nasdaq Capital Market under the symbol **RXDX** . The last reported sale price of our common stock on the Nasdaq Capital Market on June 8, 2015 was \$17.90 per share.

We have granted the underwriters an option to purchase up to an additional _____ shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ _____ and the total proceeds to us, before expenses, will be \$ _____ .

Investing in our common stock involves risks. See Risk Factors on page S-6 of this prospectus supplement and in the documents incorporated by reference into this prospectus supplement and the accompanying prospectus.

Price to Public	Underwriting Discounts and	Proceeds to Ignyta
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		Commissions(1)	(before expenses)
Per Share	\$	\$	\$
Total	\$	\$	\$

(1) We have agreed to reimburse the underwriters for certain expenses in connection with this offering. See Underwriting.

Delivery of the shares of common stock will be made on or about June , 2015.

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

Joint Book-Running Managers

Credit Suisse

Jefferies

Leerink Partners

Piper Jaffray

Co-Managers

Cantor Fitzgerald & Co.

Ladenburg Thalmann & Co.

The date of this prospectus supplement is June , 2015.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-ii
<u>PROSPECTUS SUPPLEMENT SUMMARY</u>	S-1
<u>RISK FACTORS</u>	S-6
<u>CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	S-8
<u>USE OF PROCEEDS</u>	S-9
<u>DILUTION</u>	S-10
<u>MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS</u>	S-11
<u>UNDERWRITING</u>	S-15
<u>LEGAL MATTERS</u>	S-20
<u>EXPERTS</u>	S-20
<u>WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE</u>	S-21

Prospectus

<u>ABOUT THIS PROSPECTUS</u>	1
<u>WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE</u>	2
<u>THE COMPANY</u>	4
<u>RISK FACTORS</u>	6
<u>CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	7
<u>USE OF PROCEEDS</u>	8
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	9
<u>DESCRIPTION OF CAPITAL STOCK</u>	10
<u>DESCRIPTION OF DEBT SECURITIES</u>	14
<u>DESCRIPTION OF WARRANTS</u>	22
<u>DESCRIPTION OF UNITS</u>	24
<u>GLOBAL SECURITIES</u>	25
<u>PLAN OF DISTRIBUTION</u>	28
<u>LEGAL MATTERS</u>	30
<u>EXPERTS</u>	30

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part is the accompanying prospectus dated March 13, 2015, included in our registration statement on Form S-3 (File No. 333-202403), along with the documents incorporated by reference, which provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or the SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. If any statement in one of these documents is inconsistent with a statement in another document having a later date for example, a document incorporated by reference in the accompanying prospectus the statement in the document having the later date modifies or supersedes the earlier statement.

This prospectus supplement and the accompanying prospectus are part of a shelf registration statement that we filed with the SEC. Under the shelf registration process, we may offer from time to time various securities, of which this offering of shares of our common stock is a part. Such registration statement also includes exhibits that provide more detail on the matters discussed in this prospectus supplement and the accompanying prospectus. You should read this prospectus supplement, the accompanying prospectus, including the information incorporated by reference, the exhibits filed with the SEC, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus supplement and the accompanying prospectus, along with the information contained in any free writing prospectus that we have authorized for use in connection with this offering. We have not authorized anyone to provide you with different or additional information. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the respective dates of those documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference in this prospectus supplement or the accompanying prospectus were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties and covenants were accurate only as of the date when made; therefore, such representations, warranties and covenants should not be relied on as accurate representations of the current state of our affairs.

When we refer to Ignyta, we, our, us and the Company in this prospectus, we mean Ignyta, Inc., unless otherwise specified. When we refer to you, we mean the holders of our common stock.

We have registered trademarks for Ignyta®, Methylome®, and Trailblaze®, and have pending trademark applications for Actagene, Ignyta, the Ignyta logo and design, Methylome, Oncolome, and Trailblaze. 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. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

S-ii

Table of Contents

PROSPECTUS SUPPLEMENT SUMMARY

*This summary highlights certain information about us, this offering and selected information contained elsewhere in, or incorporated by reference into, this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including our financial statements and related notes and the other information incorporated by reference into this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading *Risk Factors* in this prospectus supplement beginning on page S-6 and in the documents incorporated herein by reference.*

Company Overview

We are a precision oncology biotechnology company dedicated to discovering or acquiring, then developing and commercializing, targeted new drugs for cancer patients whose tumors harbor specific molecular alterations, as well as novel chemotherapeutics that can potentially provide additional benefit to cancer patients. We are pursuing an integrated therapeutic and diagnostic, or Rx/Dx, strategy, where we anticipate pairing 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 who are most likely to benefit from the precisely targeted drugs we develop.

Our current development plans focus on our pipeline of product candidates:

entrectinib, formerly called RXDX-101, a small molecule tyrosine kinase inhibitor directed to the Trk family tyrosine kinase receptors (TrkA, TrkB and TrkC), ROS1 and ALK proteins, which is in two Phase I/II clinical studies in molecularly defined patient populations for the treatment of solid tumors;

RXDX-105, a small molecule inhibitor of BRAF, EGFR and RET kinases that is currently in a Phase I/II clinical trial for the treatment of solid tumors;

RXDX-106, a small molecule, pseudo-irreversible inhibitor of TAM (Tyro-3, Axl and Mer) and cMET kinases that is in late preclinical development;

RXDX-107, a small molecule nanoformulation of a modified bendamustine with potential activity in solid tumors that is in late preclinical development;

RXDX-103, a small molecule inhibitor of the cell division cycle 7-related, or Cdc7, protein kinase that is currently at the development candidate stage; and

RXDX-108, a small molecule inhibitor of the atypical kinase PKC δ that is in preclinical studies. We also have rights to next generation PKC δ inhibitors in addition to the lead compound.

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

We acquired exclusive global development and marketing rights to entrectinib under a license agreement with Nerviano Medical Sciences S.r.l., or NMS, that became effective in November 2013, we acquired exclusive

S-1

Table of Contents

global development and marketing rights to RXDX-103 under a license agreement with NMS that became effective in August 2014, and we acquired our RXDX-105, RXDX-106, RXDX-107 and RXDX-108 development programs in an asset purchase transaction with Cephalon, Inc., an indirect wholly owned subsidiary of Teva Pharmaceutical Industries Ltd., or Teva, in March 2015. We are also pursuing our Spark discovery-stage programs, directed to emerging oncology targets identified through the mining of proprietary and publicly available tumor samples.

We currently pursue a two-pronged strategy to leverage the biomarker insights that we have gained, 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 driver, 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-licenses of entrectinib from NMS in November 2013 and RXDX-103 from NMS in August 2014. We believe that entrectinib 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. Entrectinib 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. A variation on this approach would be to in-license a promising product candidate that has not been developed as a specifically-targeted agent, and then utilize the expertise of our team to identify specific patient-selection hypotheses using biomarkers.

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 suitable product candidate(s) that targets that specific driver, 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 multiple molecular targets that appear to be commonly altered in different cancer tissues. We have prioritized several of these targets and have initiated target validation and drug discovery activities against some of them.

We may also, from time to time, become aware of available oncology assets that we believe we could optimally position using our Rx/Dx expertise. These assets may have been developed without a biomarker strategy, failed in clinical trials due to lack of sufficient efficacy or been deprioritized for strategic reasons. This approach is exemplified by the acquisition of our RXDX-105, RXDX-106, RXDX-107 and RXDX-108 development programs from Teva in March 2015.

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, including several cancer therapeutics. In addition, we have a laboratory registered under the Clinical Laboratory Improvement Amendments of 1988. Our personnel can use their expertise and our laboratory facilities to develop biomarker-based molecular assays to precisely define the patient populations in which we would test our product candidates, screen patients for enrollment in our clinical trials and potentially perform commercial companion diagnostic testing should any of our product candidates obtain marketing approval.

Table of Contents

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.

Recent Developments

On May 30, 2015, we presented interim results from our two Phase I clinical trials of entrectinib in poster presentations, including a poster discussion, at the 2015 Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois.

The clinical trials included the ALKA-372-001 study and the STARTRK-1 study, which is the first of our Studies Targeting Alterations Responsive to Targeted Receptor Kinase inhibition. Both trials were designed to determine the maximum tolerated dose and/or recommended Phase II dose, as well as preliminary anti-cancer activity, of single agent entrectinib in patients with solid tumors with the relevant molecular alterations: NTRK1 (encoding TrkA), ROS1 or ALK for ALKA-372-001 and NTRK1/2/3 (encoding TrkA/TrkB/TrkC), ROS1 or ALK for STARTRK-1.

As of May 1, 2015, which was the data cut-off for the presentation, the interim results showed:

A total of 67 patients with a range of solid tumors had been dosed across both clinical trials;

Entrectinib was well tolerated to date, with no treatment-related serious adverse events. Most treatment-related adverse events have been Grade 1 or Grade 2 and reversible. There was no evidence of cumulative adverse events, hepatic or renal toxicity, or QTc prolongation. Other safety findings to date included:

- i In the ALKA-372-001 study, two Grade 3 treatment-related adverse events were observed: asthenia and muscle weakness, each of which subsided with dose reduction. The most frequent adverse events were paresthesia, nausea, myalgia, asthenia, dysgeusia, and vomiting; and
- i In the STARTRK-1 study, three Grade 3 treatment-related adverse events were observed: neutropenia, which resolved with dose reduction, and two dose-limiting toxicities of reversible cognitive impairment and fatigue, both of which occurred at 800 mg fixed dose and resolved upon study drug interruption. The most frequent adverse events were fatigue, dysgeusia, constipation, nausea, and paresthesia;

Pharmacokinetic measurements showed dose-proportional increases across the daily dosing regimens evaluated, with a half-life compatible with once-daily dosing;

The body surface area (BSA)-based recommended Phase II dose was determined to be 400 mg/m² once per day (QD); both studies are continuing in order to determine a fixed daily dose regimen;

11 patients across both clinical trials met our expected Phase II eligibility criteria, which include:

- i Presence of NTRK1/2/3, ROS1 or ALK fusions, as opposed to other types of molecular alterations (e.g., SNPs, amplifications, deletions);
- i ALK inhibitor and/or ROS1 inhibitor naïve; and
- i Treatment at or above the recommended Phase II dose of 400 mg/m²; and

S-3

Table of Contents

The response rate in the 11 patients that met these criteria across both studies was 91% (10 of 11 responses as assessed by the clinical sites), with nine patients remaining on study treatment with durable responses of up to 16 treatment cycles. The responses included:

- i three of three responses in patients with NTRK1/2/3 fusions, including patients with non-small cell lung cancer, or NSCLC, colorectal cancer and acinic cell cancer;

- i five of six responses, including one complete response, in patients with ROS1 fusions, all of which were in NSCLC; and

- i two of two responses in patients with ALK fusions, including one NSCLC patient and one patient with another solid tumor.

Corporate Information

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, we merged with and into a wholly-owned subsidiary of Ignyta, Inc., or Parent, a Nevada corporation previously named Infinity Oil & Gas Company. 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. On May 20, 2013, we completed our acquisition of Actagene Oncology, Inc., or Actagene, which merged with and into our company on that date.

On June 12, 2014, we merged with and into Parent, with Ignyta surviving the merger, resulting in our reincorporation from Nevada to Delaware. In connection with this merger, each share of Parent common stock was converted into one share of Ignyta common stock, and we changed our name to Ignyta, Inc. Our principal executive offices are located at 11111 Flintkote Avenue, San Diego, California 92121, and our telephone number is (858) 255-5959.

Table of Contents

THE OFFERING

Common stock offered by us	shares.
Common stock to be outstanding immediately after this offering	shares.
Option to purchase additional shares	We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to additional shares of our common stock.
Use of proceeds	We intend to use the net proceeds from this offering to fund research and development activities for our development programs including, but not limited to, the clinical development of entrectinib, clinical and pre-clinical development of other pipeline assets such as RXDX-105, RXDX-106, RXDX-107, RXDX-103, RXDX-108 and our Spark discovery programs, and for working capital and general corporate purposes. See the section entitled <i>Use of Proceeds</i> on page S-9 of this prospectus supplement.
Risk Factors	Investing in our common stock involves a high degree of risk. See <i>Risk Factors</i> beginning on page S-6 of this prospectus supplement, as well as those <i>Risk Factors</i> incorporated by reference into this prospectus supplement, for a discussion of factors you should consider carefully before deciding to purchase any shares of our common stock.
Nasdaq Capital Market symbol	RXDX
The number of shares of our common stock to be outstanding immediately after this offering is based on 25,250,185 shares of our common stock outstanding as of March 31, 2015. The number of shares outstanding as of March 31, 2015 excludes:	

79,516 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2015, at a weighted average exercise price of \$5.78 per share;

3,962,913 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2015, at a weighted average exercise price of \$6.87 per share;

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90,000 shares of common stock issuable upon the exercise of restricted stock units outstanding as of March 31, 2015; and

1,250,396 shares of common stock reserved for future issuance under our 2014 stock incentive plan as of March 31, 2015.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their option to purchase up to an additional shares of our common stock.

S-5

Table of Contents

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors described below and the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus supplement, and all other information contained or incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and the related notes, as updated by our subsequent filings under the Exchange Act, and in any free writing prospectus that we have authorized for use in connection with this offering before acquiring any of our common stock. These risks could have a material and adverse impact on our business, results of operations, financial condition and growth prospects, which may cause the trading price of our common stock to decline and you could lose all or part of your investment.

Risks Relating to this Offering

If you purchase shares of our common stock sold in this offering, you will experience immediate and substantial dilution in the net tangible book value of your shares. In addition, we may issue additional equity or convertible debt securities in the future, which may result in additional dilution to investors.

The offering price per share of our common stock in this offering is substantially higher than the net tangible book value per share of our outstanding common stock. Investors purchasing shares of our common stock in this offering will pay a price that substantially exceeds the value of our tangible assets after subtracting liabilities. As a result, investors will incur immediate dilution of \$ per share, representing the difference in the pro forma net tangible book value per share of our common stock as of March 31, 2015 after giving effect to the offering of shares of common stock at the public offering price of \$ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. See the section entitled **Dilution** below for a more detailed discussion of the dilution you will incur if you purchase shares of our common stock in this offering.

In addition, to the extent we need to raise additional capital in the future and we issue additional shares of common stock or securities convertible or exchangeable for our common stock, our then existing stockholders may experience dilution and the new securities may have rights senior to those of our common stock offered in this offering.

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

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled **Use of Proceeds**, and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. We expect to use the net proceeds from this offering to fund research and development activities for our development programs, and for working capital and general corporate purposes. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

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.

Sales of a substantial number of our shares of common stock in the public markets, or the perception that such sales could occur, could depress the market price of our shares of common stock and impair our ability to raise capital through the sale of additional equity securities. A substantial number of our outstanding shares of

S-6

Table of Contents

common stock are, and the shares of common stock being offered by this prospectus supplement will be, freely tradable, without restriction, in the public market. Any sales of these shares or any perception in the market that such sales may occur could also cause the trading price of our common stock to decline.

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

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 one or more ownership changes as a result of our October 31, 2013 merger transaction, our November 2013, March 2014 and March 2015 common stock offerings, our March 2015 transaction with Teva, and/or this common stock offering, and we may experience one or more ownership changes as a result of future transactions in our stock. We have not performed, nor do we have any current plan to perform, a formal study of such potential limitations on the use of our net operating loss carryforwards and other tax assets under Section 382. 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, 2014, we had federal and state net operating loss carryforwards of approximately \$33.0 million and \$32.1 million, respectively, that could be limited if the merger, the common stock offerings or the Teva transaction resulted in an ownership change, or if we experience any other ownership change, which could potentially result in increased future tax liability to us.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein, and any free writing prospectus that we have authorized for use in connection with this offering, contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements other than statements of historical facts contained in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as may, will, should, expect, plan, anticipate, could, intend, target, project, contemplates, believes, estimates, predicts, potential or negative of these terms or other similar expressions. The forward-looking statements in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus supplement and are subject to a number of risks, uncertainties and assumptions, including those under the heading Risk Factors in this prospectus supplement and in the documents incorporated by reference herein, and elsewhere in this prospectus supplement. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Table of Contents

USE OF PROCEEDS

We estimate that we will receive net proceeds of approximately \$ million from the sale of the shares of common stock offered in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase up to additional shares in full, we estimate that the net proceeds of the shares we sell in this offering will be approximately \$ million.

We intend to use the net proceeds from this offering to fund research and development activities for our development programs including, but not limited to, the clinical development of entrectinib, clinical and pre-clinical development of other pipeline assets such as RXDX-105, RXDX-106, RXDX-107, RXDX-103, RXDX-108 and our Spark discovery programs, and for working capital and general corporate purposes.

The amounts and timing of our actual expenditures will depend on numerous factors, including the factors described under **Risk Factors** in this prospectus supplement, the accompanying prospectus and in the documents incorporated by reference herein, as well as the amount of cash used in our operations. We may find it necessary or advisable to use the net proceeds for other purposes, and we will have broad discretion in the application of the net proceeds. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

Table of Contents**DILUTION**

If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the net tangible book value per share of our common stock immediately after this offering. The net tangible book value of our common stock as of March 31, 2015 was approximately \$86.3 million, or approximately \$3.42 per share of common stock based upon 25,250,185 shares outstanding. Net tangible book value per share is equal to our total tangible assets, less our total liabilities, divided by the total number of shares outstanding as of March 31, 2015.

After giving effect to the issuance and sale by us of _____ shares of our common stock at the public offering price of \$ _____ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of March 31, 2015 would have been \$ _____ million, or \$ _____ per share of our common stock. This represents an immediate increase in net tangible book value of \$ _____ per share to our existing stockholders and an immediate dilution in net tangible book value of \$ _____ per share to new investors in this offering.

The following table illustrates this calculation on a per share basis:

Offering price per share		\$
Net tangible book value per share as of March 31, 2015	\$ 3.42	
Increase in net tangible book value per share attributable to the offering		
As adjusted net tangible book value per share after giving effect to the offering		
Dilution in net tangible book value per share to new investors in this offering		\$

If the underwriters exercise in full their option to purchase up to _____ additional shares of common stock at the public offering price of \$ _____ per share, the pro forma net tangible book value after this offering would be \$ _____ per share of our common stock, representing an increase of pro forma net tangible book value of \$ _____ per share to our existing stockholders and an immediate dilution of \$ _____ per share to new investors purchasing shares in this offering.

The number of shares of our common stock to be outstanding immediately after this offering is based on 25,250,185 shares of our common stock outstanding as of March 31, 2015. The number of shares outstanding as of March 31, 2015 excludes:

79,516 shares of common stock issuable upon the exercise of warrants outstanding as of March 31, 2015, at a weighted average exercise price of \$5.78 per share;

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3,962,913 shares of common stock issuable upon the exercise of stock options outstanding as of March 31, 2015, at a weighted average exercise price of \$6.87 per share;

90,000 shares of common stock issuable upon the exercise of restricted stock units outstanding as of March 31, 2015; and

1,250,396 shares of common stock reserved for future issuance under our 2014 stock incentive plan as of March 31, 2015.

The foregoing table does not give effect to the exercise of any outstanding options or warrants. To the extent options and warrants are exercised, there may be further dilution to new investors.

S-10

Table of Contents

MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES

TO NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the U.S. Internal Revenue Code of 1986, as amended (the Code), Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (the IRS), in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

U.S. expatriates and former citizens or long-term residents of the United States;

persons subject to the alternative minimum tax;

persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;

banks, insurance companies, and other financial institutions;

brokers, dealers or traders in securities;

controlled foreign corporations, passive foreign investment companies, and corporations that accumulate earnings to avoid U.S. federal income tax;

partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);

tax-exempt organizations or governmental organizations;

persons deemed to sell our common stock under the constructive sale provisions of the Code;

persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and

tax-qualified retirement plans.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND

Table of Contents

DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a Non-U.S. Holder is any beneficial owner of our common stock that is neither a U.S. person nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

an individual who is a citizen or resident of the United States;

a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;

an estate, the income of which is subject to U.S. federal income tax regardless of its source; or

a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more United States persons (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

If we make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under Sale or Other Taxable Disposition.

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN or W-8BEN-E (or other applicable documentation) certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the required documentation, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively

connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation for U.S. federal income tax purposes also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

S-12

Table of Contents

Sale or Other Taxable Disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);

the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or

our common stock constitutes a U.S. real property interest ("USRPI") by reason of our status as a U.S. real property holding corporation ("USRPHC") for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated rates. A Non-U.S. Holder that is a corporation for U.S. federal income tax purposes also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is regularly traded, as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually and constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding potentially applicable income tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the applicable withholding agent does not have actual knowledge or reason to know the holder is a United States person and the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN, W-8BEN-E or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was

actually withheld. In addition, proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above and does not have actual knowledge or reason to know that such holder is a United States person, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Table of Contents

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act, or "FATCA") on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution or a non-financial foreign entity (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any substantial United States owners (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain specified United States persons or United States owned foreign entities (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

Under the applicable Treasury Regulations, withholding under FATCA generally applies to payments of dividends on our common stock, and will apply to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2017.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Table of Contents**UNDERWRITING**

Under the terms and subject to the conditions contained in an underwriting agreement dated the date of this prospectus supplement, we have agreed to sell to the underwriters named below, for whom Credit Suisse Securities (USA) LLC, Jefferies LLC, Leerink Partners LLC and Piper Jaffray & Co. are acting as representatives, the following respective numbers of shares of common stock:

Name	Number of Shares
Credit Suisse Securities (USA) LLC	
Jefferies LLC	
Leerink Partners LLC	
Piper Jaffray & Co.	
Cantor Fitzgerald & Co.	
Ladenburg Thalmann & Co. Inc.	

The underwriting agreement provides that the underwriters are obligated to purchase all the shares of common stock in the offering if any are purchased, other than those shares covered by the option to purchase additional shares described below. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may be increased or the offering may be terminated.

We have granted to the underwriters a 30-day option to purchase on a pro rata basis up to _____ additional shares at the public offering price less the underwriting discounts and commissions.

The underwriters propose to offer the shares of common stock initially at the public offering price on the cover page of this prospectus supplement and to selling group members at that price less a selling concession of up to \$ _____ per share. After the public offering the representatives may change the public offering price and selling concession.

The following table summarizes the compensation and estimated expenses we will pay:

	Per Share		Total	
	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares	Without Option to Purchase Additional Shares	With Option to Purchase Additional Shares
Underwriting discounts and commissions payable by us	\$	\$	\$	\$
Expenses payable by us	\$	\$	\$	\$

The representatives have informed us that they do not expect sales to accounts over which the underwriters have discretionary authority to exceed 5% of the shares of common stock being offered.

We have agreed that we will not (i) offer, sell, issue, contract to sell, pledge or otherwise dispose of, (ii) offer, sell, issue, contract to sell, contract to purchase or grant any option, right or warrant to purchase, (iii) enter into any swap, hedge or any other agreement that transfers, in whole or in part, the economic consequences of ownership, (iv) establish or increase a put equivalent position or liquidate or decrease a call equivalent position or (v) file with the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to take any such action, without the prior written consent of Credit Suisse Securities (USA) LLC, for 90 days after the date of this prospectus supplement, subject to certain exceptions.

S-15

Table of Contents

The restrictions in the foregoing paragraph do not apply to (i) the sale of shares of common stock to the underwriters pursuant to the underwriting agreement, (ii) the issuance by us of shares of common stock pursuant to the exercise of warrants or options outstanding on the date of this prospectus supplement and described in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein, (iii) the grant of equity awards to eligible participants pursuant to our employee benefit or equity incentive plans described in this prospectus supplement, the accompanying prospectus or the documents incorporated by reference herein and (iv) securities issued to one or more counterparties in connection with the consummation of a strategic partnership, joint venture, collaboration, merger or the acquisition or license of any business products or technology in an aggregate amount not exceeding five percent of our outstanding shares of common stock.

Our executive officers, directors and certain of our principal stockholders have agreed that they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, enter into a transaction that would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any of these transactions are to be settled by delivery of our common stock or other securities, in cash or otherwise, or publicly disclose the intention to make any offer, sale, pledge or disposition, or to enter into any transaction, swap, hedge or other arrangement, without, in each case, the prior written consent of Credit Suisse Securities (USA) LLC for a period of 90 days after the date of this prospectus supplement, subject to certain exceptions. We have agreed that, during such 90-day period, we will not grant or permit any release or waiver of the market stand-off restrictions to which Cephalon, Inc., one of our stockholders, is bound.

We have agreed to indemnify the underwriters against liabilities under the Securities Act or contribute to payments that the underwriters may be required to make in that respect. We have also agreed to reimburse the underwriters for expenses related to the review of this offering by the Financial Industry Regulatory Authority, Inc. and the qualification of our common stock under state securities laws, in an aggregate amount not to exceed \$.

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

The underwriters and their respective affiliates are full-service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and their respective affiliates may in the future provide financial advisory or investment banking services to us from time to time for which they expect to receive customary compensation and expense reimbursement.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers. Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

In connection with the offering, the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions and penalty bids in accordance with Regulation M under the Exchange Act.

Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

Over-allotment involves sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of

S-16

Table of Contents

shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the option to purchase additional shares. In a naked short position, the number of shares involved is greater than the number of shares in the option to purchase additional shares. The underwriters may close out any covered short position by either exercising their option to purchase additional shares and/or purchasing shares in the open market.

Syndicate covering transactions involve purchases of our common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares. If the underwriters sell more shares than could be covered by the option to purchase additional shares, a naked short position, the position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on the Nasdaq Capital Market or otherwise and, if commenced, may be discontinued at any time.

This prospectus supplement and accompanying prospectus in electronic format may be made available on the web sites maintained by one or more of the underwriters, or selling group members, if any, participating in this offering and one or more of the underwriters participating in this offering may distribute this prospectus supplement and accompanying prospectus electronically. The representatives may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters and selling group members that will make internet distributions on the same basis as other allocations.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date), shares of our common stock will not be offered to the public in that Relevant Member State prior to the publication of a prospectus in relation to the common stock which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of common stock may be made to the public in that Relevant Member State at any time:

- (a) to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- (b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the manager for any such offer; or
- (c) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3(2) of the Prospectus Directive.

S-17

Table of Contents

For the purposes of this provision, the expression an offer of common stock to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the common shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State, and the expression Prospectus Directive means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in each Relevant Member State, and the expression 2010 PD Amending Directive means Directive 2010/73/EU.

Notice to Prospective Investors in the United Kingdom

Our common stock may not be offered or sold and will not be offered or sold to any persons in the United Kingdom other than persons whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or as agent) for the purposes of their businesses and in compliance with all applicable provisions of the Financial Services and Markets Act 2000 (FSMA) with respect to anything done in relation to our common stock in, from or otherwise involving the United Kingdom.

In addition, each underwriter:

- (a) has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of section 21 of FSMA) to persons who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 or in circumstances in which section 21 of FSMA does not apply to the company; and
- (b) has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

Notice to Canadian Residents

Resale Restrictions

The distribution of our common stock in Canada is being made only on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of common stock are made. Any resale of our common stock in Canada must be made under applicable securities laws which may vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of our common stock.

Representations of Purchasers

By purchasing our common stock in Canada and accepting delivery of a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

the purchaser is entitled under applicable provincial securities laws to purchase our common stock without the benefit of a prospectus qualified under those securities laws;

where required by law, the purchaser is purchasing as principal and not as agent;

the purchaser has reviewed the text above under Resale Restrictions; and

the purchaser acknowledges and consents to the provision of specified information concerning the purchase of our common stock to the regulatory authority that by law is entitled to collect the information, including certain personal information.

S-18

Table of Contents

Rights of Action Ontario Purchasers Only

Under Ontario securities legislation, certain purchasers who purchase our common stock offered by this prospectus during the period of distribution will have a statutory right of action for damages, or while still the owner of the common stock, for rescission against us in the event that this prospectus contains a misrepresentation without regard to whether the purchaser relied on the misrepresentation. The right of action for damages is exercisable not later than the earlier of 180 days from the date the purchaser first had knowledge of the facts giving rise to the cause of action and three years from the date on which payment is made for the common stock. The right of action for rescission is exercisable not later than 180 days from the date on which payment is made for the common stock. If a purchaser elects to exercise the right of action for rescission, the purchaser will have no right of action for damages against us. In no case will the amount recoverable in any action exceed the price at which our common stock was offered to the purchaser and if the purchaser is shown to have purchased our common stock with knowledge of the misrepresentation, we will have no liability. In the case of an action for damages, we will not be liable for all or any portion of the damages that are proven to not represent the depreciation in value of our common stock as a result of the misrepresentation relied upon. These rights are in addition to, and without derogation from, any other rights or remedies available at law to an Ontario purchaser. The foregoing is a summary of the rights available to an Ontario purchaser. Ontario purchasers should refer to the complete text of the relevant statutory provisions.

Enforcement of Legal Rights

All of our directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon us or those persons. All or a substantial portion of our assets and the assets of those persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against us or those persons in Canada or to enforce a judgment obtained in Canadian courts against us or those persons outside of Canada.

Taxation and Eligibility for Investment

Canadian purchasers of common stock should consult their own legal and tax advisors with respect to the tax consequences of an investment in our common stock in their particular circumstances and about the eligibility of our common stock for investment by the purchaser under relevant Canadian legislation.

Table of Contents

LEGAL MATTERS

Latham & Watkins LLP, San Diego, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Ignyta, Inc. The underwriters are being represented in connection with this offering by Cooley LLP, San Diego, California.

EXPERTS

The financial statements of the Company incorporated in this prospectus supplement by reference to the Annual Report on Form 10-K for the year ended December 31, 2014 have been audited by Mayer Hoffman McCann P.C., an independent registered public accounting firm as set forth in their report thereon. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

S-20

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Room of the SEC at prescribed rates. Further information on the operation of the SEC's Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our web site address is www.ignyta.com. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus supplement or the accompanying prospectus.

This prospectus supplement is part of a registration statement on Form S-3 that we filed with the SEC and does not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided above. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC's Public Reference Room in Washington, D.C. or through the SEC's website, as provided above.

Incorporation by Reference

The SEC's rules allow us to incorporate by reference information into this prospectus supplement, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus supplement and the accompanying prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus supplement to the extent that a statement contained in this prospectus supplement modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus supplement, between the date of this prospectus supplement and the termination of the offering of the securities described in this prospectus supplement. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus supplement and the accompanying prospectus incorporate by reference the documents set forth below that have previously been filed with the SEC:

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Our Annual Report on Form 10-K for the year ended December 31, 2014, filed with the SEC on March 12, 2015;

Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2015, filed with the SEC on May 11, 2015;

The portions of our definitive proxy statement on Schedule 14A specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 (other than information furnished rather than filed), filed with the SEC on April 30, 2015;

S-21

Table of Contents

Our Current Reports on Form 8-K (or 8-K/A) filed with the SEC on January 9, 2015, February 2, 2015, February 17, 2015, March 2, 2015, March 17, 2015 (other than information furnished rather than filed), March 17, 2015 and June 9, 2015; and

The description of our Common Stock contained in our registration statement on Form 8-A, filed with the SEC on March 11, 2014, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus supplement and deemed to be part of this prospectus supplement from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus supplement (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Ignyta, Inc.

Attn: Corporate Secretary

11111 Flintkote Avenue

San Diego, California 92121

(858) 255-5959

Exhibits to the filings will not be sent, however, unless those exhibits have specifically been incorporated by reference in this prospectus supplement and the accompanying prospectus.

Table of Contents

PROSPECTUS

IGNYTA, INC.

\$150,000,000

Common Stock

Preferred Stock

Debt Securities

Warrants

Units

We may offer and sell up to \$150,000,000 in the aggregate of the securities identified above from time to time in one or more offerings. This prospectus provides you with a general description of the securities.

Each time we offer and sell securities, we will provide a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus with respect to that offering. You should carefully read this prospectus and the applicable prospectus supplement before you invest in any of our securities.

We may offer and sell the securities described in this prospectus and any prospectus supplement to or through one or more underwriters, dealers and agents, or directly to purchasers, or through a combination of these methods. If any underwriters, dealers or agents are involved in the sale of any of the securities, their names and any applicable purchase price, fee, commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections of this prospectus entitled About this Prospectus and Plan of Distribution for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE RISK FACTORS ON PAGE 6 OF THIS PROSPECTUS AND ANY SIMILAR SECTION CONTAINED IN THE APPLICABLE PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR SECURITIES.

Our common stock is listed on the Nasdaq Capital Market under the symbol RXDX. On February 26, 2015, the last reported sale price of our common stock on the Nasdaq Capital Market was \$8.63 per share.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

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The date of this prospectus is March 13, 2015.

Table of Contents

TABLE OF CONTENTS

<u>ABOUT THIS PROSPECTUS</u>	1
<u>WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE</u>	2
<u>THE COMPANY</u>	4
<u>RISK FACTORS</u>	6
<u>CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	7
<u>USE OF PROCEEDS</u>	8
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	9
<u>DESCRIPTION OF CAPITAL STOCK</u>	10
<u>DESCRIPTION OF DEBT SECURITIES</u>	14
<u>DESCRIPTION OF WARRANTS</u>	22
<u>DESCRIPTION OF UNITS</u>	24
<u>GLOBAL SECURITIES</u>	25
<u>PLAN OF DISTRIBUTION</u>	28
<u>LEGAL MATTERS</u>	30
<u>EXPERTS</u>	30

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the U.S. Securities and Exchange Commission, or the SEC, using a shelf registration process. By using a shelf registration statement, we may sell securities from time to time and in one or more offerings up to a total dollar amount of \$150,000,000 of common stock from time to time in one or more offerings as described in this prospectus. Each time that we offer and sell securities, we will provide a prospectus supplement to this prospectus that contains specific information about the securities being offered and sold and the specific terms of that offering. The prospectus supplement may also add, update or change information contained in this prospectus with respect to that offering. If there is any inconsistency between the information in this prospectus and the applicable prospectus supplement, you should rely on the prospectus supplement. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement, together with the additional information described under the heading **Where You Can Find More Information; Incorporation by Reference**.

We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We will not make an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus and the applicable prospectus supplement to this prospectus is accurate as of the date on its respective cover, and that any information incorporated by reference is accurate only as of the date of the document incorporated by reference, unless we indicate otherwise. Our business, financial condition, results of operations and prospects may have changed since those dates.

When we refer to **Ignyta**, **we**, **our**, **us** and the **Company** in this prospectus, we mean Ignyta, Inc., unless otherwise specified. When we refer to **you**, we mean the holders of the applicable series of securities.

We have registered trademarks for Ignyta[®], Methylome[®], and Trailblaze[®], and have pending trademark applications for Actagene, Ignyta, the Ignyta logo and design, Methylome, Oncolome and Trailblaze. 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. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the [®] and symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames.

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION; INCORPORATION BY REFERENCE

Available Information

We file reports, proxy statements and other information with the SEC. Information filed with the SEC by us can be inspected and copied at the Public Reference Room maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may also obtain copies of this information by mail from the Public Reference Room of the SEC at prescribed rates. Further information on the operation of the SEC's Public Reference Room in Washington, D.C. can be obtained by calling the SEC at 1-800-SEC-0330. The SEC also maintains a web site that contains reports, proxy and information statements and other information about issuers, such as us, who file electronically with the SEC. The address of that website is <http://www.sec.gov>.

Our web site address is www.ignyta.com. The information on our web site, however, is not, and should not be deemed to be, a part of this prospectus.

This prospectus and any prospectus supplement are part of a registration statement that we filed with the SEC and does not contain all of the information in the registration statement. The full registration statement may be obtained from the SEC or us, as provided below. Forms of the indenture and other documents establishing the terms of the offered securities are or may be filed as exhibits to the registration statement. Statements in this prospectus or any prospectus supplement about these documents are summaries and each statement is qualified in all respects by reference to the document to which it refers. You should refer to the actual documents for a more complete description of the relevant matters. You may inspect a copy of the registration statement at the SEC's Public Reference Room in Washington, D.C. or through the SEC's website, as provided above.

Incorporation by Reference

The SEC's rules allow us to incorporate by reference information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The information incorporated by reference is deemed to be part of this prospectus, and subsequent information that we file with the SEC will automatically update and supersede that information. Any statement contained in a previously filed document incorporated by reference will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus modifies or replaces that statement.

We incorporate by reference our documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act in this prospectus, between the date of this prospectus and the termination of the offering of the securities described in this prospectus. We are not, however, incorporating by reference any documents or portions thereof, whether specifically listed below or filed in the future, that are not deemed filed with the SEC, including our Compensation Committee report and performance graph or any information furnished pursuant to Items 2.02 or 7.01 of Form 8-K or related exhibits furnished pursuant to Item 9.01 of Form 8-K.

This prospectus and any accompanying prospectus supplement incorporate by reference the documents set forth below that have previously been filed with the SEC:

Our Annual Report on Form 10-K for the year ended December 31, 2013, filed with the SEC on February 28, 2014.

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Our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2014, June 30, 2014 and September 30, 2014, filed with the SEC on May 12, 2014, August 12, 2014 and November 7, 2014, respectively, and Amended Quarterly Report on Form 10-Q/A for the quarter ended September 30, 2014 filed with the SEC on January 30, 2015.

Our Definitive Proxy Statement on Schedule 14A, filed with the SEC on April 30, 2014.

Table of Contents

Our Current Reports on Form 8-K filed with the SEC on January 6, 2014, January 15, 2014, February 3, 2014, February 6, 2014, February 19, 2014, February 28, 2014, April 1, 2014, April 23, 2014, May 2, 2014, May 30, 2014, June 13, 2014, July 21, 2014, August 4, 2014, August 12, 2014, September 8, 2014, October 1, 2014, December 4, 2014, December 15, 2014, January 9, 2015 and February 2, 2015.

The description of our Common Stock contained in our registration statement on Form 8-A, filed with the SEC on March 11, 2014, and any amendment or report filed with the SEC for the purpose of updating the description.

All reports and other documents we subsequently file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Exchange Act prior to the termination of this offering, including all such documents we may file with the SEC after the date of the initial registration statement and prior to the effectiveness of the registration statement, but excluding any information furnished to, rather than filed with, the SEC, will also be incorporated by reference into this prospectus and deemed to be part of this prospectus from the date of the filing of such reports and documents.

You may request a free copy of any of the documents incorporated by reference in this prospectus (other than exhibits, unless they are specifically incorporated by reference in the documents) by writing or telephoning us at the following address:

Ignyta, Inc.

Attn: Corporate Secretary

11111 Flintkote Avenue

San Diego, California 92121

(858) 255-5959

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Table of Contents

THE COMPANY

We are a precision oncology biotechnology company dedicated to discovering or acquiring, then developing and commercializing, targeted new drugs for cancer patients whose tumors harbor specific molecular alterations. We are pursuing an integrated therapeutic 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 who are most likely to benefit from the precisely targeted drugs we develop. Our current development plans focus on two product candidates: entrectinib, formerly called 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 two Phase I/II clinical studies in molecularly defined patient populations for the treatment of solid tumors; and RXDX-103, a development candidate stage inhibitor of the cell division cycle 7-related, or Cdc7, protein kinase.

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

We acquired exclusive global development and marketing rights to entrectinib under a license agreement with Nerviano Medical Sciences S.r.l., or NMS that became effective in November 2013, and we acquired exclusive global development and marketing rights to RXDX-103 under a license agreement with NMS that became effective in August 2014.

We also have our Spark discovery programs, which are directed to emerging oncology targets identified through mining of proprietary and publicly available tumor samples.

We currently pursue a two-pronged strategy to leverage the biomarker insights that we have gained, 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 driver, 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-licenses of entrectinib from NMS in November 2013 and RXDX-103 from NMS in August 2014. We believe that entrectinib 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. Entrectinib 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 RXDX-103 is one of the most advanced inhibitors of Cdc7 protein kinase, which we believe to be deregulated in several cancers, potentially including some of those that we may target with entrectinib. We believe that each of these agents has the potential to be a first-in-class drug against important molecular targets that are driving alterations in various cancers. A variation on this approach would be to in-license a promising product candidate that has not been developed as a specifically-targeted agent, then utilize the expertise of our team to identify specific patient-selection hypotheses using biomarkers.

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 suitable product candidate(s) that targets that specific driver, 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 multiple molecular targets that appear to

be commonly altered in different cancer tissues. We have prioritized several of these targets and have initiated target validation and drug discovery activities against some of them.

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

Table of Contents

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. In addition, we have a laboratory registered under the Clinical Laboratory Improvement Amendments of 1988, or CLIA. Our personnel can use their expertise and our laboratory facilities to develop biomarker-based molecular assays to precisely define the patient populations in which we would test our product candidates, screen patients for enrollment in our clinical trials and potentially perform commercial companion diagnostic testing should any of our product candidates obtain marketing approval.

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.

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, we merged with and into a wholly-owned subsidiary of Ignyta, Inc., or Parent, a Nevada corporation previously named Infinity Oil & Gas Company. 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. On May 20, 2013, we completed our acquisition of Actagene Oncology, Inc., or Actagene, which merged with and into our company on that date.

On June 12, 2014, we merged with and into Parent, with Ignyta surviving the merger, resulting in our reincorporation from Nevada to Delaware. In connection with this merger, each share of Parent common stock was converted into one share of Ignyta common stock, and we changed our name to Ignyta, Inc. Our principal executive offices are located at 11111 Flintkote Avenue, San Diego, California 92121, and our telephone number is (858) 255-5959.

Table of Contents

RISK FACTORS

Investment in any securities offered pursuant to this prospectus and the applicable prospectus supplement involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Exchange Act, and the risk factors and other information contained in the applicable prospectus supplement before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

Table of Contents

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference herein contain forward-looking statements. All statements other than statements of historical facts contained in this prospectus and the documents incorporated by reference herein are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. This prospectus and the documents incorporated by reference herein also contain estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

In some cases, you can identify forward-looking statements by terms such as may, will, should, expect, plan, anticipate, could, intend, target, project, contemplates, believes, estimates, predicts, potential or negative of these terms or other similar expressions. The forward-looking statements in this prospectus and the documents incorporated by reference herein are only predictions. We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions, including those under Risk Factors and elsewhere in this prospectus. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment. New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained in this prospectus or the documents incorporated by reference herein, whether as a result of any new information, future events, changed circumstances or otherwise.

Table of Contents

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement.

Table of Contents

RATIO OF EARNINGS TO FIXED CHARGES

If we offer preference equity securities or debt securities under this prospectus, then we will, at that time, provide a ratio of earnings to fixed charges and/or ratio of combined fixed charges and preference dividends to earnings, respectively, in the applicable prospectus supplement for such offering.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our capital stock. This description is summarized from, and qualified in its entirety by reference to, our certificate of incorporation, which has been publicly filed with the SEC. See [Where You Can Find More Information; Incorporation by Reference](#).

Our authorized capital stock consists of:

150,000,000 shares of common stock, \$0.0001 par value; and

10,000,000 shares of preferred stock, \$0.0001 par value.

Common Stock

As of December 31, 2014, there were a total of 19,584,769 shares of our common stock issued and outstanding and no shares of preferred stock issued and outstanding.

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.

Transfer Agent

The transfer agent and registrar for our common stock 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.

Preferred Stock

We currently have no outstanding shares of preferred stock. Under the terms of our second amended and restated certificate of incorporation, our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the dividend, voting and other rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or

decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Prior to the issuance of shares of each series, the board of directors is required by the General Corporation Law of the State of Delaware and our second amended and restated certificate of incorporation to adopt resolutions and file a certificate of designation with the Secretary of State of the State of Delaware. The certificate of designation fixes for each class or series the designations,

Table of Contents

powers, preferences, rights, qualifications, limitations and restrictions, including dividend rights, conversion rights, redemption privileges and liquidation preferences.

Warrants

As of December 31, 2014, there were outstanding warrants to purchase 79,517 shares of our common stock. The warrants contain customary net issuance provisions and are not callable by us.

Registration Rights

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.

Under the registration rights agreement, subject to exception in certain circumstances, we have agreed to keep such registration statement effective until 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.

Anti-Takeover Effects of Delaware Law and Our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our second amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability of our board of directors, without action by the stockholders, to issue up to 10,000,000 shares of preferred stock with voting or other rights or preferences as designated by our board of directors could impede the success of any attempt to change control of us. These and other provisions may have the effect of deferring hostile takeovers or delaying changes in control or management of our company.

Table of Contents

Stockholder Meetings

Our amended and restated bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our second amended and restated certificate of incorporation and amended and restated bylaws eliminate the right of stockholders to act by written consent without a meeting.

Staggered Board

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third-party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors

Our second amended and restated certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two-thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting

Our second amended and restated certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute

We are subject to the provisions of Section 203 of the Delaware General Corporation Law. Under Section 203, we would generally be prohibited from engaging in any business combination with any interested stockholder for a period of three years following the time that this stockholder became an interested stockholder unless:

prior to this time, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding shares owned by persons who are directors and also officers, and by employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or

Table of Contents

at or subsequent to such time, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least 66 2/3% of the outstanding voting stock that is not owned by the interested stockholder.

Under Section 203, a business combination includes:

any merger or consolidation involving the corporation and the interested stockholder;

any sale, transfer, pledge or other disposition of 10% or more of the assets of the corporation involving the interested stockholder;

any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder, subject to limited exceptions;

any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; or

the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as an entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by such entity or person.

Amendment of Charter Provisions

The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least two-thirds of the total voting power of all of our outstanding voting stock.

The provisions of Delaware law, our second amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Table of Contents

DESCRIPTION OF DEBT SECURITIES

The following description, together with the additional information we include in any applicable prospectus supplement, summarizes certain general terms and provisions of the debt securities that we may offer under this prospectus. When we offer to sell a particular series of debt securities, we will describe the specific terms of the series in a supplement to this prospectus. We will also indicate in the supplement to what extent the general terms and provisions described in this prospectus apply to a particular series of debt securities. To the extent the information contained in the prospectus supplement differs from this summary description, you should rely on the information in the prospectus supplement.

We may issue debt securities either separately, or together with, or upon the conversion or exercise of or in exchange for, other securities described in this prospectus. Debt securities may be our senior, senior subordinated or subordinated obligations and, unless otherwise specified in a supplement to this prospectus, the debt securities will be our direct, unsecured obligations and may be issued in one or more series.

The debt securities will be issued under an indenture between us and a trustee named in the prospectus supplement. We have summarized select portions of the indenture below. The summary is not complete. The form of the indenture has been filed as an exhibit to the registration statement and you should read the indenture for provisions that may be important to you. In the summary below, we have included references to the section numbers of the indenture so that you can easily locate these provisions. Capitalized terms used in the summary and not defined herein have the meanings specified in the indenture.

General

The terms of each series of debt securities will be established by or pursuant to a resolution of our board of directors and set forth or determined in the manner provided in a resolution of our board of directors, in an officer's certificate or by a supplemental indenture. (Section 2.2) The particular terms of each series of debt securities will be described in a prospectus supplement relating to such series (including any pricing supplement or term sheet).

We can issue an unlimited amount of debt securities under the indenture that may be in one or more series with the same or various maturities, at par, at a premium, or at a discount. (Section 2.1) We will set forth in a prospectus supplement (including any pricing supplement or term sheet) relating to any series of debt securities being offered, the aggregate principal amount and the following terms of the debt securities, if applicable:

the title and ranking of the debt securities (including the terms of any subordination provisions);

the price or prices (expressed as a percentage of the principal amount) at which we will sell the debt securities;

any limit on the aggregate principal amount of the debt securities;

the date or dates on which the principal on a particular series of debt securities is payable;

the rate or rates (which may be fixed or variable) per annum or the method used to determine the rate or rates (including any commodity, commodity index, stock exchange index or financial index) at which the debt securities will bear interest, the date or dates from which interest will accrue, the date or dates on which interest will commence and be payable and any regular record date for the interest payable on any interest payment date;

the place or places where principal of, and interest, if any, on the debt securities will be payable (and the method of such payment), where the debt securities of such series may be surrendered for registration of transfer or exchange, and where notices and demands to us in respect of the debt securities may be delivered;

Table of Contents

the period or periods within which, the price or prices at which and the terms and conditions upon which we may redeem the debt securities;

any obligation we have to redeem or purchase the debt securities pursuant to any sinking fund or analogous provisions or at the option of a holder of debt securities and the period or periods within which, the price or prices at which and the terms and conditions upon which the debt securities of a particular series shall be redeemed or purchased, in whole or in part, pursuant to such obligation;

the dates on which and the price or prices at which we will repurchase debt securities at the option of the holders of debt securities and other detailed terms and provisions of these repurchase obligations;

the denominations in which the debt securities will be issued, if other than denominations of \$1,000 and any integral multiple thereof;

whether the debt securities will be issued in the form of certificated debt securities or global debt securities;

the portion of principal amount of the debt securities payable upon declaration of acceleration of the maturity date, if other than the principal amount;

the currency of denomination of the debt securities, which may be United States Dollars or any foreign currency, and if such currency of denomination is a composite currency, the agency or organization, if any, responsible for overseeing such composite currency;

the designation of the currency, currencies or currency units in which payment of principal of, and premium and interest on, the debt securities will be made;

if payments of principal of, or premium or interest on, the debt securities will be made in one or more currencies or currency units other than that or those in which the debt securities are denominated, the manner in which the exchange rate with respect to these payments will be determined;

the manner in which the amounts of payment of principal of, and premium, if any, and interest on, the debt securities will be determined, if these amounts may be determined by reference to an index based on a currency or currencies or by reference to a commodity, commodity index, stock exchange index or financial index;

any provisions relating to any security provided for the debt securities;

any addition to, deletion of or change in the Events of Default described in this prospectus or in the indenture with respect to the debt securities and any change in the acceleration provisions described in this prospectus or in the indenture with respect to the debt securities;

any addition to, deletion of or change in the covenants described in this prospectus or in the indenture with respect to the debt securities;

any depositaries, interest rate calculation agents, exchange rate calculation agents or other agents with respect to the debt securities;

the provisions, if any, relating to conversion or exchange of any debt securities of such series, including if applicable, the conversion or exchange price and period, provisions as to whether conversion or exchange will be mandatory, the events requiring an adjustment of the conversion or exchange price and provisions affecting conversion or exchange;

any other terms of the debt securities, which may supplement, modify or delete any provision of the indenture as it applies to that series, including any terms that may be required under applicable law or regulations or advisable in connection with the marketing of the securities; and

whether any of our direct or indirect subsidiaries will guarantee the debt securities of that series, including the terms of subordination, if any, of such guarantees. (Section 2.2)

Table of Contents

We may issue debt securities that provide for an amount less than their stated principal amount to be due and payable upon declaration of acceleration of their maturity pursuant to the terms of the indenture. We will provide you with information on the federal income tax considerations and other special considerations applicable to any of these debt securities in the applicable prospectus supplement.

If we denominate the purchase price of any of the debt securities in a foreign currency or currencies or a foreign currency unit or units, or if the principal of, and premium, if any, and interest on, any series of debt securities is payable in a foreign currency or currencies or a foreign currency unit or units, we will provide you with information on the restrictions, elections, general tax considerations, specific terms and other information with respect to that issue of debt securities and such foreign currency or currencies or foreign currency unit or units in the applicable prospectus supplement.

Transfer and Exchange

Each debt security will be represented by either one or more global securities registered in the name of The Depository Trust Company (DTC or the Depository) or a nominee of the Depository (we will refer to any debt security represented by a global debt security as a book-entry debt security), or a certificate issued in definitive registered form (we will refer to any debt security represented by a certificated security as a certificated debt security) as set forth in the applicable prospectus supplement. Except as set forth under the heading Global Debt Securities and Book-Entry System below, book-entry debt securities will not be issuable in certificated form.

Certificated Debt Securities. You may transfer or exchange certificated debt securities at any office we maintain for this purpose in accordance with the terms of the indenture. (Section 2.4) No service charge will be made for any transfer or exchange of certificated debt securities, but we may require payment of a sum sufficient to cover any tax or other governmental charge payable in connection with a transfer or exchange. (Section 2.7)

You may effect the transfer of certificated debt securities and the right to receive the principal of, premium and interest on certificated debt securities only by surrendering the certificate representing those certificated debt securities and either reissuance by us or the trustee of the certificate to the new holder or the issuance by us or the trustee of a new certificate to the new holder.

Global Debt Securities and Book-Entry System. Each global debt security representing book-entry debt securities will be deposited with, or on behalf of, the Depository, and registered in the name of the Depository or a nominee of the Depository. Please see the section entitled Global Securities for more information.

Covenants

We will set forth in the applicable prospectus supplement any restrictive covenants applicable to any issue of debt securities. (Article IV)

No Protection in the Event of a Change of Control

Unless we state otherwise in the applicable prospectus supplement, the debt securities will not contain any provisions which may afford holders of the debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control) which could adversely affect holders of debt securities.

Table of Contents

Consolidation, Merger and Sale of Assets

We may not consolidate with or merge with or into, or convey, transfer or lease all or substantially all of our properties and assets to any person (a "successor person") unless:

we are the surviving corporation or the successor person (if other than Ignyta) is a corporation organized and validly existing under the laws of any U.S. domestic jurisdiction and expressly assumes our obligations on the debt securities and under the indenture;

immediately after giving effect to the transaction, no Default or Event of Default, shall have occurred and be continuing; and

certain other conditions are met.

Notwithstanding the above, any of our subsidiaries may consolidate with, merge into or transfer all or part of its properties to us. (Section 5.1)

Events of Default

Event of Default means with respect to any series of debt securities, any of the following:

default in the payment of any interest upon any debt security of that series when it becomes due and payable, and continuance of such default for a period of 30 days (unless the entire amount of the payment is deposited by us with the trustee or with a paying agent prior to the expiration of the 30-day period);

default in the payment of principal of any debt security of that series at its maturity;

default in the performance or breach of any other covenant or warranty by us in the indenture (other than a covenant or warranty that has been included in the indenture solely for the benefit of a series of debt securities other than that series), which default continues uncured for a period of 60 days after we receive written notice from the trustee or Ignyta and the trustee receive written notice from the holders of not less than 25% in principal amount of the outstanding debt securities of that series as provided in the indenture;

certain voluntary or involuntary events of bankruptcy, insolvency or reorganization of Ignyta;

any other Event of Default provided with respect to debt securities of that series that is described in the applicable prospectus supplement. (Section 6.1)

No Event of Default with respect to a particular series of debt securities (except as to certain events of bankruptcy, insolvency or reorganization) necessarily constitutes an Event of Default with respect to any other series of debt

securities. (Section 6.1) The occurrence of certain Events of Default or an acceleration under the indenture may constitute an event of default under certain indebtedness of ours or our subsidiaries outstanding from time to time.

We will provide the trustee written notice of any Default or Event of Default within 30 days of becoming aware of the occurrence of such Default or Event of Default, which notice will describe in reasonable detail the status of such Default or Event of Default and what action we are taking or propose to take in respect thereof. (Section 6.1)

If an Event of Default with respect to debt securities of any series at the time outstanding occurs and is continuing, then the trustee or the holders of not less than 25% in principal amount of the outstanding debt securities of that series may, by a notice in writing to us (and to the trustee if given by the holders), declare to be due and payable immediately the principal of (or, if the debt securities of that series are discount securities, that portion of the principal amount as may be specified in the terms of that series) and accrued and unpaid interest, if

Table of Contents

any, on all debt securities of that series. In the case of an Event of Default resulting from certain events of bankruptcy, insolvency or reorganization, the principal (or such specified amount) of and accrued and unpaid interest, if any, on all outstanding debt securities will become and be immediately due and payable without any declaration or other act on the part of the trustee or any holder of outstanding debt securities. At any time after a declaration of acceleration with respect to debt securities of any series has been made, but before a judgment or decree for payment of the money due has been obtained by the trustee, the holders of a majority in principal amount of the outstanding debt securities of that series may rescind and annul the acceleration if all Events of Default, other than the non-payment of accelerated principal and interest, if any, with respect to debt securities of that series, have been cured or waived as provided in the indenture. (Section 6.2) We refer you to the prospectus supplement relating to any series of debt securities that are discount securities for the particular provisions relating to acceleration of a portion of the principal amount of such discount securities upon the occurrence of an Event of Default.

The indenture provides that the trustee may refuse to perform any duty or exercise any of its rights or powers under the indenture unless the trustee receives indemnity satisfactory to it against any cost, liability or expense which might be incurred by it in performing such duty or exercising such right or power. (Section 7.1(e)) Subject to certain rights of the trustee, the holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to the debt securities of that series. (Section 6.12)

No holder of any debt security of any series will have any right to institute any proceeding, judicial or otherwise, with respect to the indenture or for the appointment of a receiver or trustee, or for any remedy under the indenture, unless:

that holder has previously given to the trustee written notice of a continuing Event of Default with respect to debt securities of that series; and

the holders of not less than 25% in principal amount of the outstanding debt securities of that series have made written request, and offered indemnity or security satisfactory to the trustee, to the trustee to institute the proceeding as trustee, and the trustee has not received from the holders of not less than a majority in principal amount of the outstanding debt securities of that series a direction inconsistent with that request and has failed to institute the proceeding within 60 days. (Section 6.7)

Notwithstanding any other provision in the indenture, the holder of any debt security will have an absolute and unconditional right to receive payment of the principal of, and premium and any interest on, that debt security on or after the due dates expressed in that debt security and to institute suit for the enforcement of payment. (Section 6.8)

The indenture requires us, within 120 days after the end of our fiscal year, to furnish to the trustee a statement as to compliance with the indenture. (Section 4.3) If a Default or Event of Default occurs and is continuing with respect to the securities of any series and if it is known to a responsible officer of the trustee, the trustee shall mail to each holder of the securities of that series notice of a Default or Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Default or Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any Default or Event of Default (except in payment on any debt securities of that series) with respect to debt securities of that series if the trustee determines in good faith that withholding notice is in the interest of the holders of those debt securities. (Section 7.5)

Modification and Waiver

We and the trustee may modify, amend or supplement the indenture or the debt securities of any series without the consent of any holder of any debt security:

to cure any ambiguity, defect or inconsistency;

Table of Contents

to comply with covenants in the indenture described above under the heading Consolidation, Merger and Sale of Assets ;

to provide for uncertificated securities in addition to or in place of certificated securities;

to add guarantees with respect to debt securities of any series or secure debt securities of any series;

to surrender any of our rights or powers under the indenture;

to add covenants or Events of Default for the benefit of the holders of debt securities of any series;

to comply with the applicable procedures of the applicable depositary;

to make any change that does not adversely affect the rights of any holder of debt securities;

to provide for the issuance of and establish the form and terms and conditions of debt securities of any series as permitted by the indenture;

to effect the appointment of a successor trustee with respect to the debt securities of any series and to add to or change any of the provisions of the indenture to provide for or facilitate administration by more than one trustee; or

to comply with requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act. (Section 9.1)

We may also modify and amend the indenture with the consent of the holders of at least a majority in principal amount of the outstanding debt securities of each series affected by the modifications or amendments. We may not make any modification or amendment without the consent of the holders of each affected debt security then outstanding if that amendment will:

reduce the amount of debt securities whose holders must consent to an amendment, supplement or waiver;

reduce the rate of or extend the time for payment of interest (including default interest) on any debt security;

reduce the principal of or premium on or change the fixed maturity of any debt security or reduce the amount of, or postpone the date fixed for, the payment of any sinking fund or analogous obligation with respect to

any series of debt securities;

reduce the principal amount of discount securities payable upon acceleration of maturity;

waive a Default or Event of Default in the payment of the principal of, or premium or interest on, any debt security (except a rescission of acceleration of the debt securities of any series by the holders of at least a majority in aggregate principal amount of the then outstanding debt securities of that series and a waiver of the payment default that resulted from such acceleration);

make the principal of or premium or interest on any debt security payable in currency other than that stated in the debt security;

make any change to certain provisions of the indenture relating to, among other things, the right of holders of debt securities to receive payment of the principal of, and premium and interest on, those debt securities and to institute suit for the enforcement of any such payment and to waivers or amendments; or

waive a redemption payment with respect to any debt security. (Section 9.3)

Except for certain specified provisions, the holders of at least a majority in principal amount of the outstanding debt securities of any series may on behalf of the holders of all debt securities of that series waive our compliance with provisions of the indenture. (Section 9.2) The holders of a majority in principal amount of

Table of Contents

the outstanding debt securities of any series may on behalf of the holders of all the debt securities of such series waive any past default under the indenture with respect to that series and its consequences, except a default in the payment of the principal of, premium or any interest on any debt security of that series; provided, however, that the holders of a majority in principal amount of the outstanding debt securities of any series may rescind an acceleration and its consequences, including any related payment default that resulted from the acceleration. (Section 6.13)

Defeasance of Debt Securities and Certain Covenants in Certain Circumstances

Legal Defeasance. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, we may be discharged from any and all obligations in respect of the debt securities of any series (subject to certain exceptions). We will be so discharged upon the deposit with the trustee, in trust, of money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money or U.S. government obligations in an amount sufficient in the opinion of a nationally recognized firm of independent public accountants or investment bank to pay and discharge each installment of principal, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities.

This discharge may occur only if, among other things, we have delivered to the trustee an opinion of counsel stating that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit, defeasance and discharge had not occurred. (Section 8.3)

Defeasance of Certain Covenants. The indenture provides that, unless otherwise provided by the terms of the applicable series of debt securities, upon compliance with certain conditions:

we may omit to comply with the covenant described under the heading Consolidation, Merger and Sale of Assets and certain other covenants set forth in the indenture, as well as any additional covenants which may be set forth in the applicable prospectus supplement; and

any omission to comply with those covenants will not constitute a Default or an Event of Default with respect to the debt securities of that series (covenant defeasance).

The conditions include:

depositing with the trustee money and/or U.S. government obligations or, in the case of debt securities denominated in a single currency other than U.S. Dollars, government obligations of the government that issued or caused to be issued such currency, that, through the payment of interest and principal in accordance with their terms, will provide money in an amount sufficient in the opinion of a nationally recognized firm of

independent public accountants or investment bank to pay and discharge each installment of principal of, premium and interest on and any mandatory sinking fund payments in respect of the debt securities of that series on the stated maturity of those payments in accordance with the terms of the indenture and those debt securities; and

delivering to the trustee an opinion of counsel to the effect that we have received from, or there has been published by, the United States Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable United States federal income tax law, in either case to the effect that, and based thereon such opinion shall confirm that, the holders of the debt

Table of Contents

securities of that series will not recognize income, gain or loss for United States federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to United States federal income tax on the same amounts and in the same manner and at the same times as would have been the case if the deposit and related covenant defeasance had not occurred. (Section 8.4)

No Personal Liability of Directors, Officers, Employees or Stockholders

None of our past, present or future directors, officers, employees or stockholders, as such, will have any liability for any of our obligations under the debt securities or the indenture or for any claim based on, or in respect or by reason of, such obligations or their creation. By accepting a debt security, each holder waives and releases all such liability. This waiver and release is part of the consideration for the issue of the debt securities. However, this waiver and release may not be effective to waive liabilities under U.S. federal securities laws, and it is the view of the SEC that such a waiver is against public policy.

Governing Law

The indenture and the debt securities, including any claim or controversy arising out of or relating to the indenture or the debt securities, will be governed by the laws of the State of New York. (Section 10.10)

Table of Contents

DESCRIPTION OF WARRANTS

We may issue warrants for the purchase of shares of our common stock or preferred stock or of debt securities. We may issue warrants independently or together with other securities, and the warrants may be attached to or separate from any offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into between us and the investors or a warrant agent. The following summary of material provisions of the warrants and warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to a particular series of warrants. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. We urge you to read the applicable prospectus supplement and any related free writing prospectus, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants.

The particular terms of any issue of warrants will be described in the prospectus supplement relating to the issue. Those terms may include:

the number of shares of common stock or preferred stock purchasable upon the exercise of warrants to purchase such shares and the price at which such number of shares may be purchased upon such exercise;

the designation, stated value and terms (including, without limitation, liquidation, dividend, conversion and voting rights) of the series of preferred stock purchasable upon exercise of warrants to purchase preferred stock;

the principal amount of debt securities that may be purchased upon exercise of a debt warrant and the exercise price for the warrants, which may be payable in cash, securities or other property;

the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;

the terms of any rights to redeem or call the warrants;

the date on which the right to exercise the warrants will commence and the date on which the right will expire;

United States Federal income tax consequences applicable to the warrants; and

any additional terms of the warrants, including terms, procedures, and limitations relating to the exchange, exercise and settlement of the warrants.

Holders of equity warrants will not be entitled:

to vote, consent or receive dividends;

receive notice as stockholders with respect to any meeting of stockholders for the election of our directors or any other matter; or

exercise any rights as stockholders of Ignyta.

Each warrant will entitle its holder to purchase the principal amount of debt securities or the number of shares of preferred stock or common stock at the exercise price set forth in, or calculable as set forth in, the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

A holder of warrant certificates may exchange them for new warrant certificates of different denominations, present them for registration of transfer and exercise them at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement. Until any warrants to purchase debt securities are

Table of Contents

exercised, the holder of the warrants will not have any rights of holders of the debt securities that can be purchased upon exercise, including any rights to receive payments of principal, premium or interest on the underlying debt securities or to enforce covenants in the applicable indenture. Until any warrants to purchase common stock or preferred stock are exercised, the holders of the warrants will not have any rights of holders of the underlying common stock or preferred stock, including any rights to receive dividends or payments upon any liquidation, dissolution or winding up on the common stock or preferred stock, if any.

Table of Contents

DESCRIPTION OF UNITS

We may issue units consisting of any combination of the other types of securities offered under this prospectus in one or more series. We may evidence each series of units by unit certificates that we will issue under a separate agreement. We may enter into unit agreements with a unit agent. Each unit agent will be a bank or trust company that we select. We will indicate the name and address of the unit agent in the applicable prospectus supplement relating to a particular series of units.

The following description, together with the additional information included in any applicable prospectus supplement, summarizes the general features of the units that we may offer under this prospectus. You should read any prospectus supplement and any free writing prospectus that we may authorize to be provided to you related to the series of units being offered, as well as the complete unit agreements that contain the terms of the units. Specific unit agreements will contain additional important terms and provisions and we will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from another report that we file with the SEC, the form of each unit agreement relating to units offered under this prospectus.

If we offer any units, certain terms of that series of units will be described in the applicable prospectus supplement, including, without limitation, the following, as applicable:

the title of the series of units;

identification and description of the separate constituent securities comprising the units;

the price or prices at which the units will be issued;

the date, if any, on and after which the constituent securities comprising the units will be separately transferable;

a discussion of certain United States federal income tax considerations applicable to the units; and

any other terms of the units and their constituent securities.

Table of Contents

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in a prospectus supplement, the securities initially will be issued in book-entry form and represented by one or more global notes or global securities, or, collectively, global securities. The global securities will be deposited with, or on behalf of DTC and registered in the name of Cede & Co., the nominee of DTC. Unless and until it is exchanged for individual certificates evidencing securities under the limited circumstances described below, a global security may not be transferred except as a whole by the depository to its nominee or by the nominee to the depository, or by the depository or its nominee to a successor depository or to a nominee of the successor depository.

DTC has advised us that it is:

a limited-purpose trust company organized under the New York Banking Law;

a banking organization within the meaning of the New York Banking Law;

a member of the Federal Reserve System;

a clearing corporation within the meaning of the New York Uniform Commercial Code; and

a clearing agency registered pursuant to the provisions of Section 17A of the Exchange Act.

DTC holds securities that its participants deposit with DTC. DTC also facilitates the settlement among its participants of securities transactions, such as transfers and pledges, in deposited securities through electronic computerized book-entry changes in participants' accounts, thereby eliminating the need for physical movement of securities certificates. Direct participants in DTC include securities brokers and dealers, including underwriters, banks, trust companies, clearing corporations and other organizations. DTC is a wholly-owned subsidiary of The Depository Trust & Clearing Corporation, or DTCC. DTCC is the holding company for DTC, National Securities Clearing Corporation and Fixed Income Clearing Corporation, all of which are registered clearing agencies. DTCC is owned by the users of its regulated subsidiaries. Access to the DTC system is also available to others, which we sometimes refer to as indirect participants, that clear through or maintain a custodial relationship with a direct participant, either directly or indirectly. The rules applicable to DTC and its participants are on file with the SEC.

Purchases of securities under the DTC system must be made by or through direct participants, which will receive a credit for the securities on DTC's records. The ownership interest of the actual purchaser of a security, which we sometimes refer to as a beneficial owner, is in turn recorded on the direct and indirect participants' records. Beneficial owners of securities will not receive written confirmation from DTC of their purchases. However, beneficial owners are expected to receive written confirmations providing details of their transactions, as well as periodic statements of their holdings, from the direct or indirect participants through which they purchased securities. Transfers of ownership interests in global securities are to be accomplished by entries made on the books of participants acting on behalf of beneficial owners. Beneficial owners will not receive certificates representing their ownership interests in the global

securities, except under the limited circumstances described below.

To facilitate subsequent transfers, all global securities deposited by direct participants with DTC will be registered in the name of DTC's partnership nominee, Cede & Co., or such other name as may be requested by an authorized representative of DTC. The deposit of securities with DTC and their registration in the name of Cede & Co. or such other nominee will not change the beneficial ownership of the securities. DTC has no knowledge of the actual beneficial owners of the securities. DTC's records reflect only the identity of the direct participants to whose accounts the securities are credited, which may or may not be the beneficial owners. The participants are responsible for keeping account of their holdings on behalf of their customers.

Table of Contents

So long as the securities are in book-entry form, you will receive payments and may transfer securities only through the facilities of the depository and its direct and indirect participants. We will maintain an office or agency in the location specified in the prospectus supplement for the applicable securities, where notices and demands in respect of the securities and the indenture may be delivered to us and where certificated securities may be surrendered for payment, registration of transfer or exchange.

Conveyance of notices and other communications by DTC to direct participants, by direct participants to indirect participants and by direct participants and indirect participants to beneficial owners will be governed by arrangements among them, subject to any legal requirements in effect from time to time.

Redemption notices will be sent to DTC. If less than all of the securities of a particular series are being redeemed, DTC's practice is to determine by lot the amount of the interest of each direct participant in the securities of such series to be redeemed.

Neither DTC nor Cede & Co. (or such other DTC nominee) will consent or vote with respect to the securities. Under its usual procedures, DTC will mail an omnibus proxy to us as soon as possible after the record date. The omnibus proxy assigns the consenting or voting rights of Cede & Co. to those direct participants to whose accounts the securities of such series are credited on the record date, identified in a listing attached to the omnibus proxy.

So long as securities are in book-entry form, we will make payments on those securities to the depository or its nominee, as the registered owner of such securities, by wire transfer of immediately available funds. If securities are issued in definitive certificated form under the limited circumstances described below, we will have the option of making payments by check mailed to the addresses of the persons entitled to payment or by wire transfer to bank accounts in the United States designated in writing to the applicable trustee or other designated party at least 15 days before the applicable payment date by the persons entitled to payment, unless a shorter period is satisfactory to the applicable trustee or other designated party.

Redemption proceeds, distributions and dividend payments on the securities will be made to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC. DTC's practice is to credit direct participants' accounts upon DTC's receipt of funds and corresponding detail information from us on the payment date in accordance with their respective holdings shown on DTC records. Payments by participants to beneficial owners will be governed by standing instructions and customary practices, as is the case with securities held for the account of customers in bearer form or registered in street name. Those payments will be the responsibility of participants and not of DTC or us, subject to any statutory or regulatory requirements in effect from time to time. Payment of redemption proceeds, distributions and dividend payments to Cede & Co., or such other nominee as may be requested by an authorized representative of DTC, is our responsibility, disbursement of payments to direct participants is the responsibility of DTC, and disbursement of payments to the beneficial owners is the responsibility of direct and indirect participants.

Except under the limited circumstances described below, purchasers of securities will not be entitled to have securities registered in their names and will not receive physical delivery of securities. Accordingly, each beneficial owner must rely on the procedures of DTC and its participants to exercise any rights under the securities and the indenture.

The laws of some jurisdictions may require that some purchasers of securities take physical delivery of securities in definitive form. Those laws may impair the ability to transfer or pledge beneficial interests in securities.

DTC may discontinue providing its services as securities depository with respect to the securities at any time by giving reasonable notice to us. Under such circumstances, in the event that a successor depository is not obtained,

securities certificates are required to be printed and delivered.

Table of Contents

As noted above, beneficial owners of a particular series of securities generally will not receive certificates representing their ownership interests in those securities. However, if:

DTC notifies us that it is unwilling or unable to continue as a depository for the global security or securities representing such series of securities or if DTC ceases to be a clearing agency registered under the Exchange Act at a time when it is required to be registered and a successor depository is not appointed within 90 days of the notification to us or of our becoming aware of DTC's ceasing to be so registered, as the case may be;

we determine, in our sole discretion, not to have such securities represented by one or more global securities; or

an Event of Default has occurred and is continuing with respect to such series of securities, we will prepare and deliver certificates for such securities in exchange for beneficial interests in the global securities. Any beneficial interest in a global security that is exchangeable under the circumstances described in the preceding sentence will be exchangeable for securities in definitive certificated form registered in the names that the depository directs. It is expected that these directions will be based upon directions received by the depository from its participants with respect to ownership of beneficial interests in the global securities.

We have obtained the information in this section and elsewhere in this prospectus concerning DTC and DTC's book-entry system from sources that are believed to be reliable, but we take no responsibility for the accuracy of this information.

Table of Contents

PLAN OF DISTRIBUTION

We may sell the securities from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods or through underwriters or dealers, through agents and/or directly to one or more purchasers. The securities may be distributed from time to time in one or more transactions:

at a fixed price or prices, which may be changed;

at market prices prevailing at the time of sale;

at prices related to such prevailing market prices; or

at negotiated prices.

Each time that we sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms and conditions of the offering of such securities, including the offering price of the securities and the proceeds to us, if applicable.

Offers to purchase the securities being offered by this prospectus may be solicited directly. Agents may also be designated to solicit offers to purchase the securities from time to time. Any agent involved in the offer or sale of our securities will be identified in a prospectus supplement.

If a dealer is utilized in the sale of the securities being offered by this prospectus, the securities will be sold to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If an underwriter is utilized in the sale of the securities being offered by this prospectus, an underwriting agreement will be executed with the underwriter at the time of sale and the name of any underwriter will be provided in the prospectus supplement that the underwriter will use to make resales of the securities to the public. In connection with the sale of the securities, we or the purchasers of securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and those dealers may receive compensation in the form of discounts, concessions or commissions from the underwriters and/or commissions from the purchasers for which they may act as agent. Unless otherwise indicated in a prospectus supplement, an agent will be acting on a best efforts basis and a dealer will purchase securities as a principal, and may then resell the securities at varying prices to be determined by the dealer.

Any compensation paid to underwriters, dealers or agents in connection with the offering of the securities, and any discounts, concessions or commissions allowed by underwriters to participating dealers will be provided in the applicable prospectus supplement. Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act of 1933, as amended, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof and to reimburse those persons for certain expenses.

Any common stock will be listed on the Nasdaq Capital Market, but any other securities may or may not be listed on a national securities exchange. To facilitate the offering of securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of the securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than were sold to them. In these circumstances, these persons would cover such over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option, if any. In addition, these persons may stabilize or maintain the price of the securities by bidding for or

Table of Contents

purchasing securities in the open market or by imposing penalty bids, whereby selling concessions allowed to dealers participating in the offering may be reclaimed if securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of the securities at a level above that which might otherwise prevail in the open market. These transactions may be discontinued at any time.

If indicated in the applicable prospectus supplement, underwriters or other persons acting as agents may be authorized to solicit offers by institutions or other suitable purchasers to purchase the securities at the public offering price set forth in the prospectus supplement, pursuant to delayed delivery contracts providing for payment and delivery on the date or dates stated in the prospectus supplement. These purchasers may include, among others, commercial and savings banks, insurance companies, pension funds, investment companies and educational and charitable institutions. Delayed delivery contracts will be subject to the condition that the purchase of the securities covered by the delayed delivery contracts will not at the time of delivery be prohibited under the laws of any jurisdiction in the United States to which the purchaser is subject. The underwriters and agents will not have any responsibility with respect to the validity or performance of these contracts.

We may engage in at the market offerings into an existing trading market in accordance with Rule 415(a)(4) under the Securities Act. In addition, we may enter into derivative transactions with third parties, or sell securities not covered by this prospectus to third parties in privately negotiated transactions. If the applicable prospectus supplement so indicates, in connection with those derivatives, the third parties may sell securities covered by this prospectus and the applicable prospectus supplement, including in short sale transactions. If so, the third party may use securities pledged by us or borrowed from us or others to settle those sales or to close out any related open borrowings of stock, and may use securities received from us in settlement of those derivatives to close out any related open borrowings of stock. The third party in such sale transactions will be an underwriter and, if not identified in this prospectus, will be named in the applicable prospectus supplement (or a post-effective amendment). In addition, we may otherwise loan or pledge securities to a financial institution or other third party that in turn may sell the securities short using this prospectus and an applicable prospectus supplement. Such financial institution or other third party may transfer its economic short position to investors in our securities or in connection with a concurrent offering of other securities.

The specific terms of any lock-up provisions in respect of any given offering will be described in the applicable prospectus supplement.

The underwriters, dealers and agents may engage in transactions with us, or perform services for us, in the ordinary course of business for which they receive compensation.

Table of Contents

LEGAL MATTERS

Latham & Watkins LLP, San Diego, California, will pass upon certain legal matters relating to the issuance and sale of the securities offered hereby on behalf of Ignyta, Inc. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Ignyta, Inc. incorporated by reference in Ignyta, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2013 have been audited by Mayer Hoffman McCann P.C., independent registered public accounting firm, as set forth in their report thereon incorporated by reference therein, and incorporated herein by reference. Such consolidated financial statements are, and audited consolidated financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the reports of Mayer Hoffman McCann P.C. pertaining to such consolidated financial statements as of the respective dates (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

Table of Contents