

Ignyta, Inc.
 Form 424B5
 October 18, 2017
Table of Contents

Filed Pursuant to Rule 424(b)(5)
 Registration No. 333-221004

This prospectus supplement relates to an effective registration statement under the Securities Act of 1933, but is not complete and may be changed. Neither this prospectus supplement nor the accompanying prospectus is an offer to sell these securities, and we are not soliciting an offer to buy these securities, in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated October 18, 2017

Prospectus supplement

(To prospectus dated October 18, 2017)

\$125,000,000

Common stock

We are offering \$125,000,000 of shares of our common stock.

Our common stock is listed on The NASDAQ Capital Market under the symbol **RXDX** . On October 17, 2017, the last reported sale price of our common stock on The NASDAQ Capital Market was \$14.35 per share. Based on an assumed public offering price of \$14.35 per share, and the last reported sale price of our common stock on the NASDAQ Capital Market on October 17, 2017, we would expect to offer approximately 8.7 million shares hereby.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions(1)	\$	\$
Proceeds to Ignyta, Inc. before expenses	\$	\$

(1) See **Underwriting** for a description of the compensation payable to the underwriters.

We have granted the underwriters an option for a period of 30 days to purchase up to \$18,750,000 additional shares of our common stock.

Investing in our common stock involves a high degree of risk. See Risk factors beginning on page S-7 of this prospectus supplement.

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 supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares of common stock to purchasers on or about October , 2017.

J.P. Morgan

Jefferies

October , 2017

Table of Contents

Table of contents

Prospectus supplement	Page
<u>About this prospectus supplement</u>	S-1
<u>Prospectus supplement summary</u>	S-3
<u>Risk factors</u>	S-7
<u>Cautionary note regarding forward-looking statements</u>	S-9
<u>Use of proceeds</u>	S-10
<u>Dilution</u>	S-11
<u>Material U.S. federal income tax consequences to Non-U.S. Holders</u>	S-12
<u>Underwriting</u>	S-16
<u>Legal matters</u>	S-26
<u>Experts</u>	S-26
<u>Where you can find more information; incorporation by reference</u>	S-26
Prospectus	Page
<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>Forward-looking statements</u>	7
<u>Use of proceeds</u>	8
<u>Ratio of earnings to fixed charges</u>	9
<u>Dividend policy</u>	10
<u>Description of capital stock</u>	11
<u>Description of debt securities</u>	15
<u>Description of other securities</u>	23
<u>Global securities</u>	24
<u>Selling securityholders</u>	27
<u>Plan of distribution</u>	27
<u>Legal matters</u>	27
<u>Experts</u>	27

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 this offering of common stock 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 October 18, 2017, included in our registration statement on Form S-3 (File No. 333-221004), along with the documents incorporated by reference, which provides more general information, some of which may not apply to this offering. 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 contained 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, as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended. 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, and the underwriters have not, authorized anyone to provide you with different or additional information. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. 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, unless we indicate otherwise. 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, our company, us and the Company in this prospectus, we mean Ignyta, Inc., a Delaware corporation, unless otherwise specified. When we refer to you, we mean the holders of our common stock.

Table of Contents

We have registered trademarks in the United States for Ignyta[®], the Ignyta word mark and design, the Ignyta design, Methylome[®], and Trailblaze[®], and have pending trademark applications in the United States for Ignyta , the Ignyta word mark and design, the Ignyta design, Oncolome , Pharos , Trailblaze , Trailblaze Pharos and Trailblaze Pharos word mark and design . We have registered trademarks in the European Union, or EU, for Ignyta[®], the Ignyta design, Methylome[®], Oncolome[®], Pharos[®], Trailblaze[®], Trailblaze Pharos[®] and Trailblaze Pharos word mark and design. We have pending trademark applications for the Ignyta word mark in Australia, Canada, China, Hong Kong, Japan, Republic of Korea (South), Singapore, Switzerland, and Taiwan. 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**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-7 and in the documents incorporated herein by reference.

Company overview

We are a biotechnology company focused on precision medicine in oncology. Our goal is not just to shrink tumors, but to eradicate residual disease—the source of cancer relapse and recurrence—in precisely defined patient populations. We are pursuing an integrated therapeutic, or Rx, and companion diagnostic, or Dx, strategy for treating patients with cancer. Our Rx efforts are focused on in-licensing or acquiring, then developing and commercializing molecularly or immunologically targeted therapies that, sequentially or in combination, are foundational for eradicating residual disease. Our Dx efforts aim to pair these product candidates with biomarker-based companion diagnostics that are designed to precisely identify, on a molecular or immunological basis, the patients who are most likely to benefit from the precision therapies we develop.

Our current pipeline includes the following compounds:

entrectinib, formerly called RXDX-101, a CNS-active, potent, and selective small molecule tyrosine kinase inhibitor of the TRK (tropomyosin receptor kinase) family of tyrosine kinase receptors (TRKA, TRKB and TRKC) and ROS1 proteins, which is in a Phase 2 clinical study and two Phase 1 clinical studies in molecularly defined adult patient populations for the treatment of solid tumors, and a Phase 1/1b clinical study in pediatric patients with advanced solid tumor malignancies;

RXDX-105, an orally bioavailable, small molecule tyrosine kinase inhibitor of RET that spares the vascular endothelial growth factor receptor, or VEGFR, which has completed enrollment in a Phase 1b clinical trial;

taladegib, an orally bioavailable, small molecule hedgehog/smoothened antagonist that has achieved clinical proof-of-concept and a recommended Phase 2 dose in a Phase 1 dose escalation trial; and

RXDX-106, a novel small molecule immunomodulatory agent with potent anti-tumor activity, alone and in combination with checkpoint inhibitors, that appears to restore and enhance overall immune function by reversing immunosuppression of innate immune cells in the tumor microenvironment (TME) through TYRO3, AXL, and MER (TAM) receptor tyrosine kinase (RTK) inhibition that is in late preclinical development.

A kinase is an 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 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.

Table of Contents

We acquired exclusive global development and commercialization rights to entrectinib under a license agreement with Nerviano Medical Sciences S.r.l., or NMS, that became effective in November 2013; we acquired our RXDX-105 and RXDX-106 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; and we acquired exclusive, global development and commercialization rights to taladegib under a license agreement with Eli Lilly and Company, or Lilly, in November 2015, which agreement was subsequently amended and restated in March 2017. In connection with such amendment and restatement, we announced our intention to explore strategic options for the taladegib program in basal cell carcinoma.

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 development and management team. 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 accredited by the College of American Pathologists and certified under the Clinical Laboratory Improvement Amendments of 1988. Our personnel use their expertise and our laboratory facilities with the goal of developing biomarker-based molecular and immunological 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 and the associated companion diagnostic 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 discovery, and developing drug 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 October 18, 2017, we announced updated results from our clinical trials, including the STARTRK-2 study of entrectinib.

In this interim analysis, entrectinib demonstrated a 78% confirmed objective response rate (ORR) (by Investigator; 95% CI: 60.0, 90.7) and a 69% confirmed ORR (by Blinded Independent Central Review, or BICR; 95% CI: 50.0, 83.9) in 32 patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that harbored ROS1 fusions. Entrectinib demonstrated compelling duration of response in these patients, with a median duration of response (mDOR) of 28.6 months (by BICR; 95% CI: 6.8, 34.8; median follow-up of 12.9 months) and a median progression free survival (mPFS) of 29.6 months (by BICR; 95% CI: 7.7, 36.6; median follow-up of 8.5 months). Of the patients evaluated, 11 had central nervous system (CNS) metastases at baseline as assessed by Investigator, and 83% (5 out of 6; by BICR) of the patients with measurable CNS metastases at presentation had confirmed intracranial RECIST responses to treatment with entrectinib.

Table of Contents

Safety was consistent with previous studies of entrectinib. With over 200 patients treated at the recommended phase 2 dose, most adverse events (AEs) were Grade 1-2 and reversible, and only 3% of patients discontinued from the study due to treatment-related AEs (TRAEs). The most common TRAEs were dysgeusia (38%), fatigue (29%), constipation (23%), dizziness (23%), and increased weight (19%). The most common Grade 3 TRAEs were increased weight (5%), anemia (4%), and fatigue (3%). There were no Grade 4 events occurring in greater than 1% of patients and no Grade 5 TRAEs.

In addition to these data in ROS1-positive NSCLC, entrectinib has demonstrated promising preliminary antitumor activity across NTRK-positive solid tumors.

On October 16, 2017, we announced that the European Medicines Agency (EMA) has granted Priority Medicines (PRIME) designation for entrectinib for the treatment of NTRK fusion-positive, locally advanced or metastatic solid tumors in adult and paediatric patients who have either progressed following prior therapies or who have no acceptable standard therapy. Through the PRIME initiative, we will have enhanced EMA support, including optimizing the entrectinib development pathway and potentially accelerating assessment of the Marketing Authorisation Application (MAA). PRIME designation for entrectinib was substantially based on data from the Phase 2 global study, STARTRK-2. In addition to PRIME designation, we have received breakthrough therapy designation (BTD) from the U.S. Food and Drug Administration (FDA) for NTRK fusion-positive, locally advanced or metastatic solid tumors in adult and pediatric patients who have either progressed following prior therapies or who have no acceptable standard therapy.

We expect to announce top-line registration-enabling data in 2018 and, based on recent guidance from the FDA, we are on track for dual NDA submissions in both the NTRK tissue-agnostic and the ROS1-positive NSCLC indications in 2018.

Corporate information

We are incorporated in the state of Delaware and were founded in 2011 (with the name NexDx, Inc.). We changed our name to Ignyta, Inc. on October 8, 2012. Our principal executive offices are located at 4545 Towne Centre Court, San Diego, California 92121, and our telephone number is (858) 255-5959.

Table of Contents**The offering**

Common stock offered by us shares (or full) shares if the underwriters exercise their option to purchase additional shares in

Common stock to be outstanding immediately after this offering shares (or full) shares if the underwriters exercise their option to purchase additional shares in

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 and pre-commercialization activities of entrectinib, the conduct of ongoing clinical and pre-clinical development of other pipeline assets, the completion of development activities related to the diagnostic lab, and for working capital and other general corporate purposes. See the section entitled **Use of proceeds** on page S-10 of this prospectus supplement.

Risk factors Investing in our common stock involves a high degree of risk. See **Risk factors** beginning on page S-7 of this prospectus supplement, as well as those **Risk factors** 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 56,237,915 shares of our common stock outstanding as of June 30, 2017. The number of shares outstanding as of June 30, 2017 excludes:

5,732,219 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2017, at a weighted-average exercise price of \$8.20 per share;

231,520 shares of common stock issuable upon the exercise of restricted stock units outstanding as of June 30, 2017;

153,472 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2017, at a weighted-average exercise price of \$5.75 per share; and

2,565,595 shares of common stock reserved for future issuance under our Amended and Restated 2014 Incentive Award Plan as of June 30, 2017.

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.

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 Securities Exchange Act of 1934, as amended, or 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, our common stock and our business

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 June 30, 2017 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 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 and pre-commercialization activities of entrectinib, the conduct of ongoing clinical and pre-clinical development of other pipeline assets, the completion of development activities related to the diagnostic lab, and for working capital and other 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 in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. These investments may not yield a favorable return to our stockholders. If

Table of Contents

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 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 Sections 382 and 383 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, March 2015, June 2015, May 2016 and May 2017 common stock offerings, our March 2015 transaction with Teva and our November 2015 transaction with Lilly, and we may experience one or more ownership changes as a result of this common stock offering and/or 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. 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, 2016, we believe we had federal and state net operating loss carryforwards of approximately \$192.3 million and \$138.8 million, respectively. These net operating loss carryforwards could be limited if the merger, the common stock offerings or the Teva and Lilly transactions resulted in an ownership change, or if we experience any other ownership change, which could potentially result in increased future tax liability to us. In addition, we are reporting an uncertain tax position in respect of approximately \$83.3 million of our California state net operating loss carryforward as of December 31, 2016, which carryforward would be disallowed under a recent decision by the California Supreme Court on apportionment, unless there is a change in law to the contrary.

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. 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 these forward-looking statements by the use of words or phrases such as believe, may, could, will, estimate, continue, anticipate, intend, seek, plan, expect, should or would, or the negative of these terms or other comparable terminology. 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 \$117.1 million from the sale of \$125.0 million of the shares of our common stock offered in this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase up to \$18.75 million of additional shares in full, we estimate that the net proceeds of the shares we sell in this offering will be approximately \$134.8 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 and pre-commercialization activities of entrectinib, the conduct of ongoing clinical and pre-clinical development of other pipeline assets, the completion of development activities related to the diagnostic lab, and for working capital and other 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 June 30, 2017 was approximately \$114.9 million, or approximately \$2.04 per share of common stock based upon 56,237,915 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 June 30, 2017.

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 June 30, 2017 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:

Public offering price per share	\$
Net tangible book value per share as of June 30, 2017	\$ 2.04
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 56,237,915 shares of our common stock outstanding as of June 30, 2017. The number of shares outstanding as of June 30, 2017 excludes:

5,732,219 shares of common stock issuable upon the exercise of stock options outstanding as of June 30, 2017, at a weighted-average exercise price of \$8.20 per share;

231,520 shares of common stock issuable upon the exercise of restricted stock units outstanding as of June 30, 2017;

153,472 shares of common stock issuable upon the exercise of warrants outstanding as of June 30, 2017, at a weighted-average exercise price of \$5.75 per share; and

2,565,595 shares of common stock reserved for future issuance under our Amended and Restated 2014 Incentive Award Plan as of June 30, 2017.

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.

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, or the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service, or 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;

tax-qualified retirement plans; and

qualified foreign pension funds as defined in Section 897(1)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds.

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.

S-12

Table of Contents

THIS DISCUSSION IS FOR INFORMATION 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 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

Table of Contents

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.

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, or USRPI, by reason of our status as a U.S. real property holding corporation, or 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

Table of Contents

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.

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 and administrative guidance, 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, 2019.

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

We are offering the shares of common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC and Jefferies LLC are acting as book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
Jefferies LLC	
Total	

The underwriters are committed to purchase all the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$ _____ per share. After the public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters' right to reject any order in whole or in part.

The underwriters have an option to buy up to _____ additional shares of common stock from us. The underwriters have 30 days from the date of this prospectus supplement to exercise this option. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ _____ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	Without option exercise	With full option exercise
Per share	\$ _____	\$ _____
Total	\$ _____	\$ _____

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$365,000. We have agreed to reimburse the underwriters for up to \$25,000 for expenses relating to the clearance of this offering with the Financial Industry Regulatory Authority, Inc.

Table of Contents

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters 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 representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not, subject to specified exceptions, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act relating to, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, without the prior written consent of J.P. Morgan Securities LLC for a period of 90 days after the date of this prospectus supplement.

Our directors and executive officers, and certain of our significant securityholders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, subject to specified exceptions, for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of J.P. Morgan Securities LLC, (1) lend, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, or other securityholders in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition, or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock. We have agreed to indemnify the several underwriters against certain liabilities, including liabilities under the Securities Act.

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

In connection with this offering, the underwriters may engage in stabilizing transactions, which involve making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involve the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are

Table of Contents

concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discounts and commissions received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Capital Market, in the over-the-counter market or otherwise.

In addition, in connection with this offering certain of the underwriters (and selling group members) may engage in passive market making transactions in our common stock on The NASDAQ Capital Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The NASDAQ Capital Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement may not be offered or sold, directly or indirectly, nor may this prospectus supplement or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement. This prospectus supplement does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus supplement in any jurisdiction in which such an offer or a solicitation is unlawful.

Table of Contents

United Kingdom

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). The securities are only available to, and any invitation, offer or agreement to subscribe for, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

European Economic Area

In relation to each member state of the European Economic Area, no offer of securities which are the subject of the offering has been, or will be made to the public in that Member State, other than under the following exemptions under the Prospectus Directive:

to any legal entity which is a qualified investor as defined in the Prospectus Directive;

to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the underwriters for any such offer; or

in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of securities referred to in (a) to (c) above shall result in a requirement for the Company or the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive, or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person located in a Member State to whom any offer of securities is made or who receives any communication in respect of any offer of ordinary shares, or who initially acquires any securities will be deemed to have represented, warranted, acknowledged and agreed to and with the underwriters and the Company that (1) it is a qualified investor within the meaning of the law in that Member State implementing Article 2(1)(e) of the Prospectus Directive; and (2) in the case of any securities acquired by it as a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, the securities acquired by it in the offer have not been acquired on behalf of, nor have they been acquired with a view to their offer or resale to, persons in any Member State other than qualified investors, as that term is defined in the Prospectus Directive, or in circumstances in which the prior consent of the underwriters has been given to the offer or resale; or where ordinary shares have been acquired by it on behalf of persons in any Member State other than qualified investors, the offer of those ordinary shares to it is not treated under the Prospectus Directive as having been made to such persons.

The Company, the underwriters and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgments and agreements.

This prospectus has been prepared on the basis that any offer of securities in any Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of securities. Accordingly any person making or intending to make an offer in that Member State of securities which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of securities in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

Table of Contents

For the purposes of this provision, the expression an offer of securities to the public in relation to any securities in any Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State, the expression Prospectus Directive means Directive 2003/71/EC (as amended) and includes any relevant implementing measure in each Member State.

Canada

The common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Switzerland

The securities offered by this prospectus supplement may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, us, the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Dubai International Financial Centre (DIFC)

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority (DFSA). This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no

Table of Contents

responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

United Arab Emirates

The securities offered by this prospectus supplement have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus supplement does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus supplement has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Australia

This prospectus supplement:

does not constitute a disclosure document under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the Corporations Act);

has not been, and will not be, lodged with the Australian Securities and Investments Commission (ASIC), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document under Chapter 6D.2 of the Corporations Act; and

may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, or Exempt Investors, available under section 708 of the Corporations Act.

The securities offered by this prospectus supplement may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the securities may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any securities may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the securities, you represent and warrant to us that you are an Exempt Investor.

As any offer of securities under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the securities you undertake to us that you will not, for a period of 12 months from the date of issue of the securities, offer, transfer, assign or otherwise alienate those securities to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Table of Contents

Japan

The securities offered by this prospectus supplement have not been and will not be registered under the Financial Instruments and Exchange Act. Accordingly, the securities may not be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan.

Hong Kong

The securities offered by this prospectus supplement have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

WARNING

The contents of this document have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than:

to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA);

to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA; or

otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

Table of Contents

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

where no consideration is or will be given for the transfer;

where the transfer is by operation of law;

as specified in Section 276(7) of the SFA; or

as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Bermuda

The securities offered by this prospectus supplement may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

Saudi Arabia

This prospectus supplement may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority (CMA) pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended (the CMA Regulations). The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

British Virgin Islands

The securities are not being, and may not be offered to the public or to any person in the British Virgin Islands for purchase or subscription by or on behalf of us. The securities may be offered to companies incorporated under the BVI Business Companies Act, 2004 (British Virgin Islands), BVI Companies), but only where the offer will be made to, and received by, the relevant BVI Company entirely outside of the British Virgin Islands.

This prospectus supplement has not been, and will not be, registered with the Financial Services Commission of the British Virgin Islands. No registered prospectus has been or will be prepared in respect of the securities for the purposes of the Securities and Investment Business Act, 2010 (SIBA) or the Public Issuers Code of the British Virgin Islands.

The securities may be offered to persons located in the British Virgin Islands who are qualified investors for the purposes of SIBA. Qualified investors include (i) certain entities which are regulated by the Financial

Table of Contents

Services Commission in the British Virgin Islands, including banks, insurance companies, licensees under SIBA and public, professional and private mutual funds; (ii) a company, any securities of which are listed on a recognised exchange; and (iii) persons defined as professional investors under SIBA, which is any person (a) whose ordinary business involves, whether for that person's own account or the account of others, the acquisition or disposal of property of the same kind as the property, or a substantial part of our property; or (b) who has signed a declaration that he, whether individually or jointly with his spouse, has net worth in excess of US\$1,000,000 and that he consents to being treated as a professional investor.

China

This prospectus supplement does not constitute a public offer of the securities offered by this prospectus supplement, whether by sale or subscription, in the People's Republic of China (the PRC). The securities are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the securities without obtaining all prior PRC's governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this document are required by the issuer and its representatives to observe these restrictions.

Korea

The securities have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder (the FSCMA), and the securities have been and will be offered in Korea as a private placement under the FSCMA. None of the securities may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder (the FETL). The securities have not been listed on any of securities exchanges in the world including, without limitation, the Korea Exchange in Korea. Furthermore, the purchaser of the securities shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the securities. By the purchase of the securities, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the securities pursuant to the applicable laws and regulations of Korea.

Malaysia

No prospectus or other offering material or document in connection with the offer and sale of the securities has been or will be registered with the Securities Commission of Malaysia (Commission) for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Malaysia other than (i) a closed end fund approved by the Commission; (ii) a holder of a Capital Markets Services Licence; (iii) a person who acquires the securities, as principal, if the offer is on terms that the securities may only be acquired at a consideration of not less than RM250,000 (or its equivalent in foreign currencies) for each transaction; (iv) an individual whose total net personal assets or total net joint assets with his or her spouse exceeds RM3 million (or its equivalent in foreign currencies), excluding the value of the primary residence of the individual; (v) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign

Table of Contents

currencies) per annum in the preceding twelve months; (vi) an individual who, jointly with his or her spouse, has a gross annual income of RM400,000 (or its equivalent in foreign currencies), per annum in the preceding twelve months; (vii) a corporation with total net assets exceeding RM10 million (or its equivalent in a foreign currencies) based on the last audited accounts; (viii) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies); (ix) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010; (x) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010; and (xi) any other person as may be specified by the Commission; provided that, in the each of the preceding categories (i) to (xi), the distribution of the securities is made by a holder of a Capital Markets Services Licence who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus supplement is subject to Malaysian laws. This prospectus supplement does not constitute and may not be used for the purpose of public offering or an issue, offer for subscription or purchase, invitation to subscribe for or purchase any securities requiring the registration of a prospectus with the Commission under the Capital Markets and Services Act 2007.

Taiwan

The securities have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the securities in Taiwan.

South Africa

Due to restrictions under the securities laws of South Africa, the securities are not offered, and the Offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions applies:

the offer, transfer, sale, renunciation or delivery is to duly registered banks, mutual banks, financial services provider, financial institution, the Public Investment Corporation (in each case registered as such in South Africa), a person who deals with securities in their ordinary course of business, or a wholly owned subsidiary of a bank, mutual bank, authorized services provider or financial institution, acting as agent in the capacity of an authorized portfolio manager for a pension fund (duly registered in South Africa), or as manager for a collective investment scheme (registered in South Africa); or

the contemplated acquisition cost of the securities, for any single addressee acting as principal is equal to or greater than R1,000,000. This document does not, nor is it intended to, constitute an *offer to the public* (as that term is defined in the South African Companies Act, 2008 (the SA Companies Act) and does not, nor is it intended to, constitute a prospectus prepared and registered under the SA Companies Act. This document is not an *offer to the public* and must not be acted on or relied on by persons who do not fall within Section 96(1)(a) of the SA Companies Act (such persons being referred to as relevant persons). Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

A South African resident person or company or any non-South African company which is a subsidiary of a South African company is not permitted to acquire the securities unless such person has obtained exchange control approval to do so.

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 Ignyta, Inc. as of December 31, 2016, and for the year ended December 31, 2016, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing.

The financial statements of Ignyta, Inc. incorporated in this prospectus supplement by reference to Ignyta, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2015 have been audited by Mayer Hoffman McCann P.C., an independent registered public accounting firm, as set forth in their report included therein, and incorporated herein by reference. 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.

Where you can find more information; incorporation by reference

Available information

We file annual, quarterly and current 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 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

Table of Contents

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 Exchange Act, 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:

our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the SEC on March 14, 2017;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017, filed with the SEC on May 1, 2017 and August 8, 2017, respectively;

our Current Reports on Form 8-K filed with the SEC on January 11, 2017, February 9, 2017, February 15, 2017, March 23, 2017, March 30, 2017, April 4, 2017, April 27, 2017, May 9, 2017, May 16, 2017, June 7, 2017, June 15, 2017, August 18, 2017, September 6, 2017, September 11, 2017, October 17, 2017 and October 18, 2017;

our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed), filed with the SEC on April 28, 2017; 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

4545 Towne Centre Court

San Diego, California 92121

(858) 255-5959

Edgar Filing: Ignyta, Inc. - Form 424B5

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.

S-27

Table of Contents

PROSPECTUS

IGNYTA, INC.

Common Stock

Preferred Stock

Debt Securities

Depository Shares

Warrants

Units

Rights

We may offer and sell the securities identified above, and any selling securityholders may offer and sell shares of common stock identified above, in each case from time to time in one or more offerings. This prospectus provides you with a general description of the securities. We will not receive any proceeds from the sale of our common stock by any selling securityholders.

Each time we or any of the selling securityholders offer and sell securities, we or such selling securityholders will provide a supplement to this prospectus that contains specific information about the offering and, if applicable, the selling securityholders, as well as 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, together with the documents we incorporate by reference, 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. In addition, any selling securityholders may offer and sell shares of our common stock from time to time, together or separately. 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.

Our common stock is listed on the Nasdaq Capital Market under the symbol **RXDX** . On October 17, 2017, the last reported sale price of our common stock was \$14.35 per share.

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.

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.

The date of this prospectus is October 18, 2017

Table of Contents

TABLE OF CONTENTS

	Page
<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>Forward-Looking Statements</u>	7
<u>Use of Proceeds</u>	8
<u>Ratio of Earnings to Fixed Charges</u>	9
<u>Dividend Policy</u>	10
<u>Description of Capital Stock</u>	11
<u>Description of Debt Securities</u>	15
<u>Description of Other Securities</u>	23
<u>Global Securities</u>	24
<u>Selling Securityholders</u>	27
<u>Plan of Distribution</u>	27
<u>Legal Matters</u>	27
<u>Experts</u>	27

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, as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended, 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 of common stock as described in this prospectus. Each time that we or the selling securityholders offer and sell securities, we or the selling securityholders 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. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement or free writing prospectus 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 or free writing prospectus, you should rely on the prospectus supplement or free writing prospectus, as applicable. Before purchasing any securities, you should carefully read both this prospectus and the applicable prospectus supplement (and any applicable free writing prospectuses), together with the additional information described under the heading **Where You Can Find More Information; Incorporation by Reference**.

Neither we, nor the selling securityholders, have authorized anyone to provide you with any information or to make any representations other than those contained in this prospectus, any applicable prospectus supplement or any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We and the selling securityholders take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the selling securityholders 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 only as of the date on its respective cover, that the information appearing in any applicable free writing prospectus is accurate only as of the date of that free writing prospectus, 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 in the United States for Ignyta[®], the Ignyta word mark and design, the Ignyta design, Methylome[®], and Trailblaze[®], and have pending trademark applications in the United States for Ignyta , the Ignyta word mark and design, the Ignyta design, Oncolome , Pharos , Trailblaze , Trailblaze Pharos and Trailblaze Pharos word mark and design . We have registered trademarks in the European Union, or EU, for Ignyta[®], the Ignyta design, Methylome[®], Oncolome[®], Pharos[®], Trailblaze[®], Trailblaze Pharos[®] and Trailblaze Pharos word mark and design. We have pending trademark applications for the Ignyta word mark in Australia, Canada, China, Hong Kong, Japan, Republic of Korea (South), Singapore, Switzerland, and Taiwan. 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 website 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 website address is www.ignyta.com. The information on our website, 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, 2016, filed with the SEC on March 14, 2017;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017, filed with the SEC on May 1, 2017 and August 8, 2017, respectively;

our Current Reports on Form 8-K filed with the SEC on January 11, 2017, February 9, 2017, February 15, 2017, March 23, 2017, March 30, 2017, April 4, 2017, April 27, 2017, May 9, 2017, May 16, 2017, June 7, 2017, June 15, 2017, August 18, 2017, September 6, 2017, September 11, 2017, October 17, 2017 and October 18, 2017;

Table of Contents

our Definitive Proxy Statement on Schedule 14A (other than information furnished rather than filed), filed with the SEC on April 28, 2017; 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, 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

4545 Towne Centre Court

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 and any accompanying prospectus supplement.

Table of Contents

THE COMPANY

We are a biotechnology company focused on precision medicine in oncology. Our goal is not just to shrink tumors, but to eradicate residual disease – the source of cancer relapse and recurrence – in precisely defined patient populations. We are pursuing an integrated therapeutic, or Rx, and companion diagnostic, or Dx, strategy for treating patients with cancer. Our Rx efforts are focused on in-licensing or acquiring, then developing and commercializing molecularly or immunologically targeted therapies that, sequentially or in combination, are foundational for eradicating residual disease. Our Dx efforts aim to pair these product candidates with biomarker-based companion diagnostics that are designed to precisely identify, on a molecular or immunological basis, the patients who are most likely to benefit from the precision therapies we develop.

Our current pipeline includes the following compounds:

entrectinib, formerly called RXDX-101, a CNS-active, potent, and selective small molecule tyrosine kinase inhibitor of the TRK (tropomyosin receptor kinase) family of tyrosine kinase receptors (TRKA, TRKB and TRKC) and ROS1 proteins, which is in a Phase 2 clinical study and two Phase 1 clinical studies in molecularly defined adult patient populations for the treatment of solid tumors, and a Phase 1/1b clinical study in pediatric patients with advanced solid tumor malignancies;

RXDX-105, an orally bioavailable, small molecule tyrosine kinase inhibitor of RET that spares the vascular endothelial growth factor receptor, or VEGFR, which has completed enrollment in a Phase 1b clinical trial;

taladegib, an orally bioavailable, small molecule hedgehog/smoothened antagonist that has achieved clinical proof-of-concept and a recommended Phase 2 dose in a Phase 1 dose escalation trial; and

RXDX-106, a novel small molecule immunomodulatory agent with potent anti-tumor activity, alone and in combination with checkpoint inhibitors, that appears to restore and enhance overall immune function by reversing immunosuppression of innate immune cells in the tumor microenvironment (TME) through TYRO3, AXL, and MER (TAM) receptor tyrosine kinase (RTK) inhibition that is in late preclinical development.

A kinase is an 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 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 commercialization rights to entrectinib under a license agreement with Nerviano Medical Sciences S.r.l., or NMS, that became effective in November 2013; we acquired our RXDX-105 and RXDX-106 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; and we acquired exclusive, global development and commercialization rights to taladegib under a license agreement with Eli Lilly and Company, or Lilly, in November 2015, which agreement was subsequently amended and restated in March 2017. In connection with such amendment and restatement, we announced our intention to explore strategic options for the taladegib

program in basal cell carcinoma.

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 development and management team. 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

Table of Contents

Drug Administration, including several cancer therapeutics. In addition, we have a laboratory accredited by the College of American Pathologists and certified under the Clinical Laboratory Improvement Amendments of 1988. Our personnel use their expertise and our laboratory facilities with the goal of developing biomarker-based molecular and immunological 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 and the associated companion diagnostic 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 discovery, and developing drug 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 are incorporated in the state of Delaware and were founded in 2011 (with the name NexDx, Inc.). We changed our name to Ignyta, Inc. on October 8, 2012. Our principal executive offices are located at 4545 Towne Centre Court, 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 our 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 in 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 and any applicable free writing prospectus 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. Please also refer to the section below entitled *Forward-Looking Statements*.*

Table of Contents

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 the documents incorporated by reference herein, 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. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. 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. For all forward-looking statements, we claim the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

Table of Contents

USE OF PROCEEDS

We intend to use the net proceeds from the sale of the securities as set forth in the applicable prospectus supplement. We will not receive any of the proceeds from the sale of common stock being offered by any of the selling securityholders.

Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES**

Our ratios of earnings to fixed charges are as follows for the periods indicated:

	Six months ended		Year ended December 31,			
	June 30,		2016	2015	2014	2013
	2017					
Ratio of earnings (loss) to fixed charges and preferred stock dividends ⁽¹⁾						

⁽¹⁾ Our earnings were inadequate to cover combined fixed charges and preferred stock dividends for the years ended December 31, 2013, 2014, 2015 and 2016 by \$14.2 million, \$40.0 million, \$92.5 million and \$103.6 million, respectively. Our earnings from continuing operations were inadequate to cover combined fixed charges and preferred stock dividends for the six months ended June 30, 2017 by \$68.4 million.

For purposes of calculating the ratio of earnings to combined fixed charges and preferred stock dividends, earnings represent net loss from continuing operations before provision for income taxes plus fixed charges. Fixed charges consist of interest expense (including amortization of debt issuance costs and debt discount) and estimated interest component of rent. For the periods indicated above, we had no outstanding shares of preferred stock with required dividend payments. Therefore, the ratios of earnings to combined fixed charges and preferred stock dividends are identical to the ratios presented in the table above.

Table of Contents

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock and do not anticipate paying any cash dividends in the foreseeable future. We expect to retain available cash to finance ongoing operations and the potential growth of our business. Any future determination to pay dividends on our common stock will be at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, business prospects and other factors our board of directors may deem relevant, and subject to the restrictions contained in any future financing instruments. In addition, our ability to pay dividends is currently restricted by the terms of a loan agreement we entered into with Oxford Finance LLC and Silicon Valley Bank in June 2016.

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 second amended and restated 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 June 30, 2017, there were a total of 56,237,915 shares of our common stock issued and outstanding and no shares of preferred stock issued and outstanding.

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

Table of Contents

Warrants

As of June 30, 2017, there were outstanding warrants to purchase 153,472 shares of our common stock. The warrants contain customary net issuance provisions and are not callable by us. These warrants have a weighted average exercise price of \$5.75 per share and expire at various dates through June 2023.

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.

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.

Table of Contents

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

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.

Table of Contents

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 or free writing prospectus, 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;

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;

Table of Contents

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 U.S. 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)

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.

Table of Contents

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 that 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) that could adversely affect holders of debt securities.

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 Event of Default shall have occurred and be continuing;
and

certain other conditions are met.

Table of Contents

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 or any debt security (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; or

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 Event of Default within 30 days of becoming aware of the occurrence of such Event of Default, which notice will describe in reasonable detail the status of such 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 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.

Table of Contents

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 that 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 an 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 an Event of Default within 90 days after it occurs or, if later, after a responsible officer of the trustee has knowledge of such Event of Default. The indenture provides that the trustee may withhold notice to the holders of debt securities of any series of any 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;

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;

Table of Contents

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 an 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 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

Table of Contents

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 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.

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 U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. 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 U.S. federal income tax purposes as a result of the deposit, defeasance and discharge and will be subject to U.S. 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 that may be set forth in the applicable prospectus supplement; and

any omission to comply with those covenants will not constitute 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 U.S. Internal Revenue Service a ruling or, since the date of execution of the indenture, there has been a change in the applicable U.S. 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 U.S. federal income tax purposes as a result of the deposit and related covenant defeasance and will be subject to U.S. 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.

Table of Contents

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 OTHER SECURITIES

We will set forth in the applicable prospectus supplement a description of any depositary shares, warrants, units or rights issued by us that may be offered and sold pursuant to this prospectus.

Table of Contents

GLOBAL SECURITIES

Book-Entry, Delivery and Form

Unless we indicate differently in any applicable prospectus supplement or free writing prospectus, 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

SELLING SECURITYHOLDERS

Information about selling securityholders, where applicable, will be set forth in a prospectus supplement, in a post-effective amendment or in filings we make with the SEC under the Exchange Act that are incorporated by reference.

PLAN OF DISTRIBUTION

We or any of the selling securityholders may sell the offered securities from time to time:

through underwriters or dealers;

through agents;

directly to one or more purchasers; or

through a combination of any of these methods of sale.

We will identify the specific plan of distribution, including any underwriters, dealers, agents or direct purchasers and their compensation in the applicable prospectus supplement.

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, the selling securityholders or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The financial statements of Ignyta, Inc. as of December 31, 2016, and for the year ended December 31, 2016, have been incorporated by reference herein and in the registration statement in reliance upon the report of KPMG LLP, independent registered public accounting firm, incorporated by reference herein, and upon the authority of said firm as experts in accounting and auditing. To the extent that KPMG LLP audits and reports on financial statements of Ignyta, Inc. issued at future dates, and consents to the use of its report thereon, such financial statements also will be incorporated by reference in the registration statement in reliance upon its report and said authority.

The financial statements of Ignyta, Inc. incorporated in this prospectus supplement by reference to Ignyta, Inc.'s Annual Report on Form 10-K for the year ended December 31, 2015 have been audited by Mayer Hoffman McCann P.C., an independent registered public accounting firm, as set forth in their report included therein, and incorporated herein by reference. 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.

Table of Contents

\$125,000,000

Common stock

Prospectus supplement

J.P. Morgan

October , 2017

Jefferies