IGNYTA, INC. (RXDX)

Leader in TrkA and Consolidator of Targeted Cancer Therapies; Phase II Readout in 2015 to Define Registration Strategy. Initiating Coverage with BUY Rating and $20.00 PT.

Investment Rating	BUY
Price Target	$20.00
Price (03/21/14)	$9.96
52 Week Range	$8.00 - $20.00
Shares Outstanding (pro forma)	20.0 MM
Market Capitalization	$198.0 MM
Cash (pro forma)	$99.0 MM
Volume (avg. daily)	79,272
S&P 500 Index (03/21/14)	1,866.52
NASDAQ Composite (03/21/14)	4,276.79

FY (December 31)	2013A	2014E	2015E
Revenues (MM)	$0.0	$0.0	$0.0
EPS (F.D.)	($3.83)	($1.15)	($1.38)

EPS (Qtr.)	1Q	2Q	3Q	4Q
2014E	($0.37)	($0.24)	($0.28)	($0.29)
2015E	($0.33)	($0.34)	($0.35)	($0.36)

Company Description

Ignyta is developing personalized oncology drugs using diagnostic tests to identify patients most likely to respond to therapy. The company's lead product, RXDX-101, is a TrkA/B/C, ROS1, ALK inhibitor in Phase I development for the treatment of solid tumors. Ignyta hopes to move the program into Phase II development in 2015 for multiple indications including NSCLC. The San Diego-based company is also in pre-clinical development of other targeted cancer therapies based on its proprietary Oncolome molecular expression database.

Investment Summary

We are initiating coverage of Ignyta Inc. (RXDX) with a BUY rating and $20.00 PT. We view the company's RXDX-101 as the most advanced Trk inhibitor in clinical development for treatment of solid tumors. Additionally, we believe RXDX has both the management expertise and financial resources to be a consolidator of targeted oncology drug candidates as many large pharmaceutical companies look to reposition oncology drug development to focus on immunotherapies such as PD-1 inhibitors and chimeric antigen receptors (CARS). Finally, the company has a promising but early-stage in-house pipeline of drug candidates against novel cancer targets. We expect RXDX-101 and potential business development to be the primary sources of value creation over the next 12-18 months. Specifically, RXDX-101 is on track to complete Phase I studies by early 2015 and begin a Phase II proof-of-concept study in multiple histologies in early 2015. We view results from the Phase II studies, which may readout before the end of 2015, to serve as a value inflection point for RXDX shares. While preclinical models suggest potential activity in a range of solid tumors, non-small cell lung cancer (NSCLC) is the primary driver for our $490M peak sales forecast and, in our view, the lowest risk path to commercialization based on the known activity of ALK inhibitors and strong biologic rationale for the role of TrkA. Additionally, we expect RXDX to remain active in business development with a focus on clinical-stage assets that have been de-prioritized as some large pharmaceuticals refocus on the larger market opportunities offered by immunotherapies. Given the company's strong balance sheet and experienced management, we believe RXDX is positioned to be a partner of choice. Lastly, we view RXDX as more than a growth-by-acquisition story. The company has assembled an experienced group of researchers to develop in-house drug candidates based on its oncolome database of genetic and epigenetic gene signatures. While these are higher risk programs with long timeline to commercialization, internal product development offers the potential for greater financial leverage than in-licensing, in our view. Our $20.00 price target is based on a DCF model with peak sales from RXDX-101 of $490M and 2022 free cash flow to RXDX of $168M.

- **A Leader in TrkA Clinical Development for Solid Tumors.** RXDX-101 is a pan-kinase inhibitor of TrkA/B/C, ALK and ROS1 that is nearing completion of Phase I studies. As such, we believe the compound is among the most advanced clinical programs targeting TrkA, a new oncogene involved in tumor cell proliferation and survival. Based on a review of scientific literature, we believe regulation of TrkA and related TrkB and TrkC receptors may result in more durable clinical responses and offer better efficacy than other second-generation targeted therapies for NSCLC. Additionally, TrkA/B/C activity has been shown to impact tumor development in several other solid tumors including colon cancer and breast cancer. We expect RXDX to explore small POC studies in multiple tumor types over the next two years.
- **"Basket Study" May Support Initiation of Pivotal Study as Early As Late 2015:** Following completion of a Phase I continuous dosing study, RXDX plans to enroll a Phase II basket study of patients with various histologies including TrkA+, TrkB+/C+, ROS1+ and ALK+ treatment failures in various solid tumor types. Our timeline calls for the basket study to begin enrolling in 1Q14 with potential identification of a population for registration studies as early as 4Q15 and potential kick off of the registration study before the end of 2015. While a basket study offers limited near term visibility on a go-to-market strategy, in our view, TrkA+ NSCLC is a potential indication based on the known activity of ALK inhibitors, biologic role of TrkA and robust pre-clinical data suggesting RXDX-101 offers significant blood-brain barrier permeability.
- **Positioned as Partner of Choice for De-prioritized Targeted Therapies:** We view the potential success of immunotherapies as a positive for RXDX. With the growing evidence of strong clinical activity for immunotherapies such as PD-1 inhibitors in multiple tumor types, we expect some pharmaceutical companies to reallocate resources away from targeted therapies, which may offer smaller market opportunities. We believe this shift offers an opportunity for companies such as RXDX that can move quickly to acquire de-prioritized programs and offer expertise in optimizing both a drug candidate and companion diagnostic.
- **$20.00 PT Based on DCF Valuation:** Our valuation model assumes a 25% discount rate, 15% long-term revenue growth rate, fully taxed terminal year (2022) FCF of $168M and fully diluted share count of 21.5 million.

Kevin DeGeeter
212.409.2027
kdegeeter@ladenburg.com

Disclosures and Analyst Certifications can be found in Appendix A.

INVESTMENT THESIS

Initiating Coverage with a BUY Rating

We are initiating coverage of RXDX with a Buy rating and $20.00 price target. We view RXDX as a hybrid targeted oncology drug development model combining internal drug discovery expertise with opportunistic product in-licensing to rapidly build a broad pipeline. In the near term we expect investors to focus on Phase I/II clinical trials of RXDX-101 in NSCLC and other solid tumors. In addition to inhibiting well validated ALK and ROS1 targets, RXDX-101 is among the most advanced drugs in development for regulating TrkA/B/C, kinases, which have been shown to be an important upstream activating target of the RAS, PI3K and MAPK pathways. Currently, there are no approved drugs targeting Trk. Based on potential activity against TrkA and evidence of blood-brain permeability, in our view, RXDX-101 is well positioned to be a front line therapy in ALK+ NSCLC patients. We expect completion of a Phase II study in late 2015 to serve as an important near catalyst for RXDX shares. Additionally, we believe the company may be a partner of choice for business development as some large pharmaceutical and biotechnology companies de-emphasize target oncology drug development in favor of immunotherapy approaches. Any future in-licensing or acquisitions could represent upside to our financial forecast. Our $20.00 PT is based on a DCF valuation assuming RXDX-101 peak sales of $490M and FCF of $168M.

Trk Emerging as an Important Target in Oncology Drug Development

The Trk family of kinase receptors - including TrkA, TrkB and TrkC - are gene rearrangements that are believed to play a role in 1) central and peripheral neuronal cell development, 2) induction of growth arrest and 3) inhibition of programmed cell death. Phosphorylation of the related thyrosine residues is known to activate the RAS, PI3K and MAPK pathways that are well characterized in cancer tumor biology. Currently, there are no approved cancer therapies targeting Trk kinases. We believe RXDX-101 is among the most advanced compounds targeting TrkA/B/C.

Data from Phase II “Basket” Study Late in 2015 to Define Regulatory Strategy

We expect completion of a Phase II basket study in patients with various histologic subtypes including TrkA+, TrkB+/TrkC+, ROS1+ and certain ALK+ populations to offer a broad first glimpse into the efficacy profile of RXDX-101 based on both molecular mechanism of action (inhibition of TrkA/B/C, ROS1 and ALK) and based on solid tumor type (NSCLC, papillary thyroid, prostate, etc.). While this study design offers less near term visibility on regulatory strategy than a traditional one mutation and one tumor type study design (i.e., ALK+ NSCLC), in our view, a basket approach is the optimal strategy for a pan-kinase inhibitor such as RXDX-101. Our timeline calls for the study to begin enrolling in 1H15 with potential identification of lead indication for a registration study based on ORR in as few as 6-10 patients with a specific histologic subtype. The timing for defining a lead indication will be data driven but could be as early as late 2015, in our view.

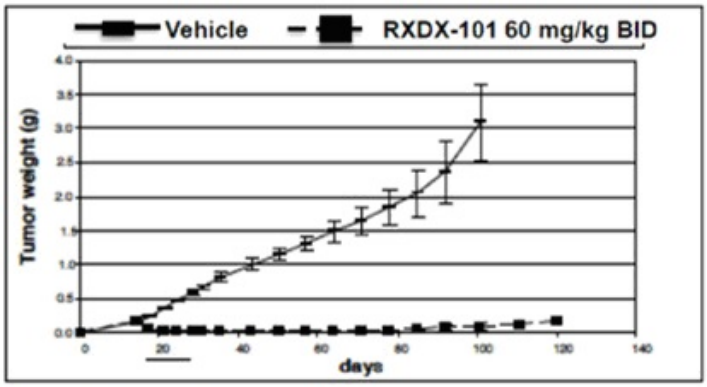
Pan-Kinase Inhibitors vs Multiple Single Kinase Inhibitors Strategy?

There is an active debate in the clinical community on whether future development of targeted cancer therapies should focus on optimizing drugs to maximize potency against a single kinase or to formulate pan-kinase inhibitors against two or more targets. RXDX-101 targets the Trk pathway through a pan-kinase inhibitor with activity against ALK, ROS1 and TrkA/B/C. Other companies are developing therapies only targeting Trk. We believe safety profile will be an important factor in settling this debate for Trk inhibitors. Preliminary Phase I data for RXDX-101 and TSR-101, a Trk inhibitor from Tesaro, suggest regulation of Trk is associated with relatively benign adverse event profile. If this profile is confirmed in larger studies, we believe a single pan-kinase inhibitor may enjoy better patient compliance than a multi-drug regimen.

$490M Peak Sales Forecast Driven by NSCLC

We do not expect RXDX to define a go to market strategy for RXDX-101 until the Phase II basket study begins to readout in 2H15. As such, there are still several moving pieces in the commercial model that limit our ability to build a traditional revenue market model. Based on the known activity of ALK inhibitors, preclinical data on the role of TrkA in NSCLC and robust pre-clinical data suggesting significant blood-brain barrier permeability, we view a subset of NSCLC patients as the most likely lead indication. We believe it is still too early to forecast whether the precise population is TrkA+ patients or patients with a combination TrkA+ and ALK+ status. Our revenue model assumes RXDX-101 and other second generation ALK inhibitors with good blood-brain barrier permeability will immediately displace crizotinib as frontline therapies for ALK+ NSCLC. As such, we see an opportunity for frontline monotherapy pricing of $10,000 per month and market opportunity of $2B+ in NSCLC. Our revenue forecast assumes RXDX-101 captures a quarter of this market and a majority market share among TrkA+ patients for peak sales of $490M. Additionally, there is scientific literature suggesting Trk status may be important in the tumor biology for a range of solid tumors including papillary thyroid cancer, pancreatic cancer and prostate cancer. Our revenue forecast does not include a contribution from any of these other opportunities. We will revisit our revenue forecast following completion of the Phase II basket study.

Table 1. An ALK-driven mouse xenograft model of human NSCLC



Source: Company Documents (2013)

Potential Partner of Choice for Larger Companies Deemphasizing Targeted Therapies

Our Buy rating for shares of RXDX is based, at least in part, on a shift of resources at many large pharmaceutical companies from targeted oncology drugs to immunotherapy. This shift is being driven by the potential for immunotherapies to offer sustained improvements in overall survival in a range of tumor types. If successful, immunotherapies offer the promise of serving larger market opportunities than targeted therapies such as RXDX-101.

As larger companies consolidate their research focus we expect some companies to outlicense promising but niche targeted therapies to smaller companies for future development. We believe RXDX is positioned to be a partner of choice based on 1) internal capacity to develop both therapeutics and companion diagnostics, 2) strong balance sheet to fund timely development and 3) experienced management team. Additionally, while oncology drug development is a highly competitive market, in our view, the shift of investment toward immunotherapies may result in a somewhat less competitive environment for companies remaining in targeted therapy. On net, we envision a transition of targeted oncology to an orphan drug-like business model based on niche patient populations, small clinical trials, and premium pricing. Importantly, we believe these markets can be served by a direct sales force, at least in the U.S.

Investment in Diagnostic Lab to Speed Time to Market; Attractive Asset to Partners

RXDX recently announced plans to build a diagnostic lab with a goal of achieving CLIA certification in 2014. If management can achieve this aggressive goal, we expect RXDX to use its own laboratory to screen patients for the Phase II U.S. clinical trial to begin in early 2015. By internalizing diagnostic development RXDX is taking control of a potential rate limiting step in future registration studies of RXDX-101. Management intends to explore use of both existing diagnostic technologies and certain in-house technologies that may offer more rapid screening of patients. Importantly, RXDX is the only well capitalized biotechnology company that we are aware of that is committed to in-house diagnostic product development. We believe this in-house diagnostic capacity may serve as an important strategic asset as RXDX continues discussions with potential partners for in-licensing of target therapies.

VALUATION: $20.00 PRICE TARGET

Our $20.00 price target for shares of RXDX is based on a discounted cash flow (DCF) model for sales of RXDX-101 in NSCLC. We do not include any contribution from RXDX-101 in other indications or the company's other pipeline programs.

Our model calls for the company to sell RXDX-101 in the United States with a field sales force of about 90 reps resulting in selling expenses of $30M-$35M annually. Outside the U.S. we expect RXDX-101 to be licensed to commercial partners with RXDX receiving net royalty of 10%. We expect the company to achieve profitability in 2019 and begin paying taxes in 2021 at an effective tax rate of 38%. Our forecast calls for RXDX-101 sales of $490M for 2022 (last year of our DCF model) with roughly 90% of revenue from U.S. sales and 10% from Europe and ROW. For the final year of our DCF valuation we forecast free cash flow of $168M driven by sales for NSCLC. Our DCF model assumes a 25% discount rate, long term revenue growth rate of 15% and share count of 21.5 million shares on a fully diluted basis.

Table 2. DCF Assumptions

Commercial DCF Assumptions	
Discount rate	25%
Long-term revenue growth	15%
Terminal year	2022
Fully diluted share count (millions)	21.5

Source: Ladenburg Thalmann estimates and Company Reports

We view a 25% discount rate, which is 2%-3% lower than our typical discount rate for an oncology company in Phase I/II development, as appropriate given the RXDX's strong balance sheet (adequate to fund business into 2017) and solid clinical validation of ALK as an important therapeutic target. Additionally, we believe RXDX has an experienced management team with a proven track record in building successful biotechnology companies.

Our 15% long term revenue growth rate is in line with our standard long term growth rate for biotechnology companies. We believe the growth rate is appropriate given RXDX's commitment to invest in internal pipeline programs beyond RXDX-101.

Our share count of 21.5 million assumes cash conversion of roughly 1.5 million options and warrants. We would note that some of these instruments contain cashless conversion features and actual future dilution may be less than the full 1.5 million shares. Our model calls for current cash balances to fund operations into 2017 with an incremental capital requirement of roughly $40M-$60M to achieve profitability. Whether the capital requirement is funded with cash conversion of options and warrants, additional debt or issuance of equity does not have a material impact on the DCF valuation, in our view.

Table 3. DCF Model

Ignyta Discounted Cash Flow Assumptions										
($ in millions)	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	TERMINAL
Operating profit	($20.9)	($27.2)	($34.7)	($41.5)	($24.2)	$81.5	$232.4	$278.0	$273.3	
Depreciation & amortization	0.3	0.6	0.7	0.8	0.9	1.1	1.2	1.4	1.5	
Taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	(107.0)	(105.5)	
Interest income - net	(0.4)	(0.4)	(0.5)	(0.7)	(0.8)	(0.8)	(0.4)	0.6	1.4	
Change in working capital	1.8	0.8	0.9	0.8	(7.2)	(22.4)	(31.5)	(9.7)	(0.0)	
Capital expenditures	(2.2)	(1.0)	(1.2)	(1.4)	(1.6)	(1.8)	(2.0)	(2.2)	(2.4)	
Total free cash flow	($21.4)	($27.3)	($34.8)	($42.0)	($33.0)	$57.5	$199.7	$161.0	$168.4	$1,683.6
Revenue growth rate	NA	NA	NA	NA	NA	309%	104%	17%	2%	15%
Discount rate	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%
Discount factor	1.0	1.0	0.8	0.6	0.5	0.4	0.3	0.3	0.2	0.2
Discounted cash flow	($21.4)	($27.3)	($27.8)	($26.8)	($16.9)	$23.6	$65.4	$42.2	$35.3	$353.1

Source: Ladenburg Thalmann estimates

POTENTIAL NEAR TERM EVENTS

For the next 12-18 months, we view presentation of Phase II data for RXDX-101 in late 2015 as the most significant milestone. For the remainder of 2014 we encourage investors to focus on potential presentation of complete Phase I data – including efficacy results from patients treated at MTD – in 2H14.

We would remind investors that the pace of Phase I enrollment for RXDX-101 decelerated during the process of licensing the compound from Nerviano. Following completion of the license agreement in November 2013, RXDX management has moved to quickly complete the Phase I program.

In February at the International Association for the Study of Lung Cancer (IASLC) meeting, investigators from Massachusetts General presented data from 18 patients enrolled in six different dose cohorts. The Phase I arm of the study is designed to enroll 20-30 patients. We believe RXDX is well positioned to complete Phase I enrollment in 2Q14.

The Phase I study is enrolling patients primarily from Italy. Last month, RXDX filed an IND with FDA to support a Phase I U.S. dose escalation clinical trial of continuous daily dosing of RXDX-101. We expect enrollment to begin in 2H14 with completion in early 2015.

The biggest unknown in evaluating upcoming milestones is the exact patient cohorts for Phase II study. RXDX has communicated plans to enroll a so-called basket study including patients with various histologies (TRKA/B/C, ROS1 and ALK) and solid tumor type (NSCLC, papillary thyroid, prostate, etc.). The study is designed to identify the optimal solid tumor type and histology for future development based on ORR. We view completion of this study – preliminary data may be available as early as 4Q15 – as a significant milestone in defining the future clinical and regulatory direction of RXDX-101.

Lastly, as noted in our investment thesis, we believe pipeline development through acquisitions is an area of potential upside to our DCF valuation. We are cautiously optimistic RXDX will complete the in-licensing or acquisition of one or more products before the end of 2015.

Table 4. Near Term Events

Expected Near-term Events		
Event	**Time**	**Importance**
Complete enrollment of Phase I intermittent dose study of RXDX-101	2Q14	Low
Present top line data for Phase I study of RXDX-101in solid tumors	2H14	High
Begin dosing for continuous dose Phase I cohorts for RXDX-101 in U.S.	2H14	Low
Begin Phase II continuous dosing cohort for RXDX-101	1H15	Low
Preliminary data from Phase II RXDX-101 study	2H15	High
In license additional compounds	2015	Medium

Source: Ladenburg Thalmann estimates

CORPORATE BACKGROUND AND BUSINESS MODEL

The company was formed in August 2011 as NexDx, Inc. to commercialize diagnostic tests based on epigenetic biomarkers for rheumatoid arthritis licensed from the University of California, San Diego. In October 2012, the company name was changed to Ignyta, Inc. and management began transitioning the business model to focus on drug development programs combining diagnostic technologies with targeted therapeutics. As part of this transition Ignyta acquired Actagene Oncology in May 2013 for 1.6 million shares of Ignyta stock. The transaction provided an internal drug discovery engine, oncolome, and key personnel that currently serve as the core of Ignyta's development team.

Following the Actagene transaction Ignyta accelerated efforts to in-license one or more clinical-stage therapeutic programs. In August 2013, Ignyta identified RXDX-101 from Nerviano Medical Sciences S.r.l. as the lead in-licensing candidate. In November 2013, the company secured the necessary funding to close on the asset purchase and simultaneously merged into a publicly traded shell company.

The licensing agreement provided RXDX with global commercial rights to RXDX-101, a tyrosine kinase inhibitor targeting TrkA/B/C, ROS1 and ALK. The program is enrolling patients in a Phase I study of molecularly defined solid tumor populations. The agreement also covers RXDX-102, a tyrosine kinase inhibitor targeting TrkA, TrkB and TrkC. The compound is in preclinical development for hematological and solid tumor indications.

In conjunction with the Nerviano licensing agreement, RXDX raised $54M in two equity private placements at $6.00 per share. On October 31, 2013, the company completed a reverse merger with Infinity Oil & Gas Co. and was listed on OTCQB Marketplace. The stock began trading under the symbol "RXDX" in December 2013 with limited liquidity due to the very small number of register shares. Shares of RXDX began regular trading in February 2014 once the registration statement became effective. In March 2014, RXDX completed a $55.3M underwritten financing and relisted on the NASDAQ National Market.

The company qualified as an "emerging growth company" under the JOBS Act and may elect to file financial statements with abbreviated disclosure of certain financial information for up to 5 years (through 2018).

BUSINESS MODEL

RXDX is focused on combining diagnostic technology with small molecule oncology drug development expertise to commercialize targeted therapies for the treatment of cancer, particularly solid tumors. We expect management to rely on a mix of in-house product development and in-licensing of early-stage drug candidates from large pharmaceutical companies. Additionally, RXDX expects to selectively license compounds that previously failed late-stage clinical trials but for which there is a strong hypothesis for pursuing future development in a subset of patients with a particular molecular signature. The company plans to rely on contract research organizations to conduct clinical trials and other third parties for manufacturing of API and finished product. We expect RXDX to commercialize its products in the U.S. while partnering in other geographies.

RXDX's oncolome platform uses multivariate biomarker analysis to identify DNA methylation signatures. The primary disease areas of focus are oncology and chronic autoimmune disorders. Once RXDX has identified a clinically interesting gene signature, management seeks to identify therapeutics targeting the relevant signature through either in-licensing (RXDX-101) or internal development (Spark-1, Spark-2 and Spark-3).

While several other companies are applying similar business models, in our view, RXDX's previous focus on diagnostic product development and experienced team of successful oncology drug development executives provides a unique mix of skills well suited for targeted oncology drug development.

As mentioned above, RXDX started as a molecular diagnostic company and has retained and expanded its molecular testing acumen to include additional senior scientists with experience creating translational applications for next-generation sequencing. We believe this deep commitment to understanding diagnostic technologies is unique among drug companies, particularly smaller biotechs, and may translate to faster time-to-market for newly identified molecular targets such as Trk. Additionally, we believe there may be an opportunity to integrate RXDX's diagnostic team into early drug discovery to identify differentiated new drug candidates. As such, we encourage investors to focus on preclinical development of RXDX's in-house Spark programs over the next 12-24 months for a clearer sense of potential synergies between the diagnostic and therapeutic groups.

Lastly, we believe management has a proven pedigree in oncology drug development and a track record of successful biotech startup experience. During the nine months since refocusing the business on drug development management has raised $109M, licensed a potential first-to-market Trk inhibitor, filed an IND to shift clinical trials from Europe to the U.S. and hired a core group of successful research and clinical development scientists. While the company is still early in its maturation, in our view, the preliminary accomplishments speak to the flexibility and expertise of RXDX's leadership team.

Table 5. Ignyta Drug Pipeline

Compound	Target	Disc	Pre-clinical	Ph 1	Ph 2	Ph 3	Mkt	Global Commercial Rights
RXDX-101	TrkA, ROS1, ALK inhibitor							Ignyta
RXDX-102	TrkA, TrkB, TrkC inhibitor							Ignyta
Spark-1 Rx/Dx Program								Ignyta
Spark-2 Rx/Dx Program								Ignyta
Spark-3 Rx/Dx Program								Ignyta

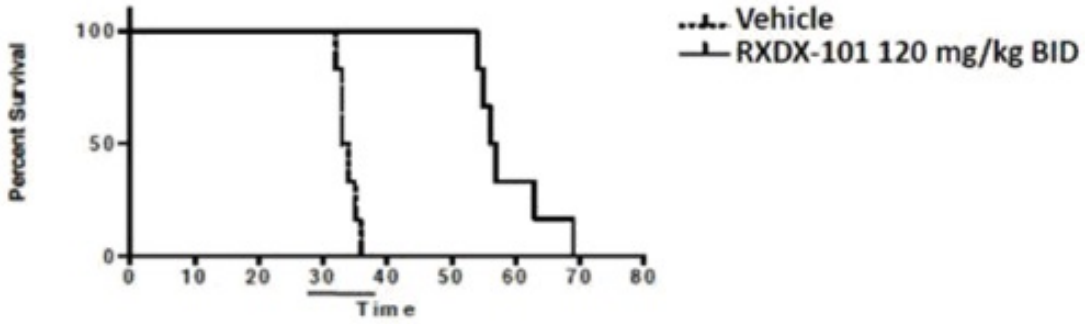
Source: Company Documents (2013)

RXDX-101 PROFILE – TRK INHIBITION OFFERS DIFFERENTIATION

RXDX-101 is the company's lead program and primary asset. The drug is a tyrosine kinase inhibitor directed to gene rearrangements, splice variants and gene expression to TrkA/B/C, ROS1 and ALK receptors. The compound was identified based on its selective binding to TrkA but also appears to inhibit TrkB and TrkC. The program is currently in Phase I development for solid tumors expressing ALK, ROS1 or TrkA/B/C variants.

The program was developed at a Pfizer research facility in Italy to optimize binding affinity for ALK and to provide coverage for a broader range of mutations. If the drug was simply a second-generation ALK inhibitor, we believe the profile would be competitive with LDK378 from Novartis and other second-generation ALK inhibitor. However, we believe the addition TrkA/B/C inhibition offers important differentiation and may support more durable clinical responses than ALK inhibitors.

Table 6. RXDX-101 Extends Life in Mouse Model of Brain Metastasis



Source: Company Documents (2013)

Pfizer and the Nerviano research group invested $20M over 5 years in the program with a goal of better understanding the crystal structure of ALK. The improved binding affinity for ROS1 is an artifact of this development approach due to the high level of homology between the two gene fusions. The net result is a compound that binds to ALK in a different manner than the first generation ALK inhibitor crizotinib and offers a 10-fold greater binding affinity for ROS1 than crizotinib.

RXDX also appears to cross the blood-brain, which would be expected to limit brain metastases (up to 50% of crizotinib refractory or relapsed patients and 20% of newly diagnosed NSCLC patients present with brain metastasis). As shown in Table 6, in a model of H2228 NSCLC cell line of ALK rearrangements injected directly into the brain parenchyma of mice, subjects treated with RXDX-101 at 60mg/kg and 120mg/kg twice daily for 10 days demonstrated a nearly 90% increase in survival (56.5 days vs 33.5 days).

Additionally, Pfizer optimized RXDX-101 to regulate TrkA based on a growing body of scientific literature suggesting TrkA dysregulation may contribute to proliferation and survival of cancer cells. The compound also appears to have binding affinity against related variants in TrkB and TrkC. It is this binding to TrkA/B/C, which, in our view, serves as the most important area of differentiation for RXDX-101.

Consistent with other small molecule products, RXDX-101 can be manufactured from widely available API and does not appear to present any notable production challenges. The compound appears to adhere to the rule of 5 for bioavailability and had a half life of 20 hours in Phase I clinical trials, which should support twice daily dosing, in our view.

In preclinical studies adverse events were variable across species with the most significant adverse events reported in a dog model including neuropathy and other CNS adverse events that did not resolve upon discontinuation of the drug.

RXDX-101 Phase I Intermittent Dosing – Strong Safety Profile

Nerviano began a Phase I 3+3 dose escalation study of RXDX-101 in patients with TrkA, ROS1 or ALK gene fusions at two sites in Italy late in 2012. The protocol called for patients to be dosed once daily for 4 days of a weekly cycle and for 3 weeks of a 4 week schedule for a total of 12 days of a 28 day cycle. A total of 11 patients were dosed prior to the program being transferred to RXDX in November 2013.

In February 2014 at the International Association for the Study of Lung Cancer (IASLC) meeting, investigators from Massachusetts General presented preliminary Phase I data suggesting a clean safety profile and signs of clinical activity. A total of 18 patients had been enrolled with 17 in six different dose cohorts receiving at least one dose. A total of 7 patients were still receiving RXDX-101. Investigators reported 2 ALK+ patients in the second dose cohort demonstrated sustained clinical response. A NSCLC patient had stable disease after 12 cycles while a neuroblastoma patient had a partial response after 13 cycles. One ROS1+ pancreatic cancer patient in the 3rd cohort had stable disease after 8 cycles.

There were no dose-limiting toxicities with only one case of Grade III toxicity (asthenia). The drug demonstrated a half life of 20 hours and pharmacokinetics consistent with BID dosing.

We view the data as promising anecdotal signs of efficacy but do not believe the dose escalation study reached an optimal dose level to make a meaningful assessment of efficacy. While the study remains open, RXDX will now look to explore continuous daily dosing under a U.S. IND. Complete Phase I data should be released at a medical meeting in 2H14.

2H14 Kick Off For Phase I Continuous Dosing Study

In February 2014, the company filed an IND for RXDX-101 in the U.S. and announced plans to initiate a new Phase I/IIa study in United States, Europe and possibly Asia. The open label study, known as STARTRK-1 (Study Targeting ALK, ROS1 or TRKA/B/C), will enroll metastatic solid tumor patients with molecular alternations in ALK, ROS1 and TrkA/B/C with a focus on enrolling a significant number of Trk+ patients.

The Phase I component will be a dose escalation study of continuous daily BID dosing of RXDX-101. We expect the cohort to begin enrolling patients in either 3Q14 or 4Q14. While RXDX-101 was not associated with any dose limiting toxicity in the Italian Phase I study, given significant differences in dose schedule (continuous dosing vs 12 days of a 28-day cycle) we expect RXDX to revisit to relatively low dose level in the continuous dosing Phase I study. As such, we expect the Phase I study to take at least six months to complete with potential presentation of top line data at ASCO in 2015.

In terms of expected adverse events, crizotinib and most of the second-generation ALK inhibitors have shown a mild dose-dependent impact on QT-prolongation. Additionally, asthenia was observed in both the Italian Phase I study of RXDX-101 and Phase I studies of TSR-011, Trk inhibitor in development at Tesaro. Additionally, given that Trk is a receptor for nerve growth factor, we would expect all Trk inhibitors to be associated with neuropathy (seen both in preclinical studies of RXDX-101 and Phase I data for TSR-011).

PHASE II POC DATA AVAILABLE AS EARLY AS END OF 2015

We view completion of a Phase II basket study in patients with various histologic subtypes including TrkA+, TrkB+/TrkC+, ROS1+ and certain ALK+ populations as a critical milestone in the development of RXDX-101.

The study will enroll patients based on histologic subtype with a secondary goal of capturing patients with a range of tumor types. We would expect RXDX to place a high priority on enrolling Trk+ patients based on demonstrated binding affinity of RXDX-101 for TrkA/B/C.

As a reminder, tyrosine kinase inhibitors typically demonstrate a rapid onset of action with most patients that respond to the drugs demonstrating tumor shrinkage in the first or second cycle of therapy. As such, we expect objective response rate (ORR) to be the primary endpoint in a Phase II with most responders identified within 1-3 months of beginning therapy.

Our timeline calls for the study to begin enrolling in 1H15 with potential to identify an indication for a registration study based on ORR in as little as 6-10 patients with a specific histologic subtype. The timing for defining an indication to graduate from the basket study will be data driven but could be as early as 4Q15, in our view.

Importantly, the study design will explore different combinations of histologic subtype and tumor types and may identify more than one indication for future registration studies.

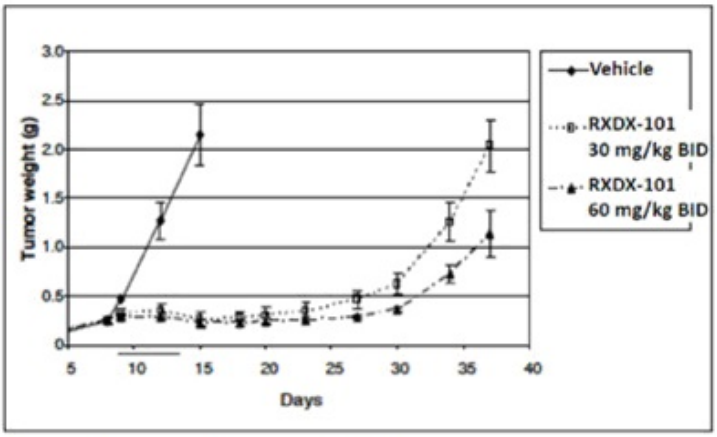
In terms of requirements for FDA clearance, we believe approval of crizotinib remains an appropriate benchmark. The drug received FDA clearance in 2011 based on 2 single-arm studies enrolling a total of 255 patients. The primary endpoint was ORR.

PRECLINICAL PROFILE OF RXDX-101

RXDX-101 completed a rigorous preclinical development program with Pfizer and Nerviano. In addition to significant manufacturing process development, the compound completed PK and efficacy studies in multiple animal models and cell lines for various solid tumors. This detailed preclinical program is the primary basis for our confidence in the potential efficacy profile RXDX-101 in tumors with TrkA gene variants.

In addition to the efficacy profile in an ALK-driven mouse xenograft model of human NSCLC highlighted in Table 1 on page 3 and impact on survival in a mouse model of H2228 NSCLC cell line of ALK rearrangements injected directly into the brain parenchyma highlighted in Table 6 on page 8, RXDX-101 has demonstrated dose-dependent activity in a TrkA-driven mouse xenograft model of human colorectal cancer. Subjects treated with RXDX-101 demonstrated control of tumor mass for up to 30 days. The 60 mg/kg dosed twice daily demonstrating a more durable control of tumor weight than 30 mg/kg dosed twice daily (see Table 7 below).

Table 7. RXDX-101 Shows Dose Response in Colon Cancer Model

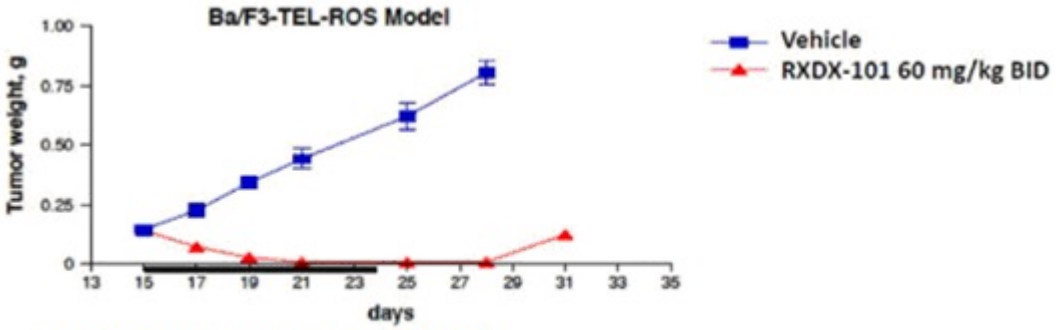


Source: Company Documents (2013)

In terms of evidence supporting permeability of blood brain barrier, RXDX-101 demonstrated very different ratios of brain/blood concentration between species from a low of 0.4 in a mouse model, to 0.6-1.0 in rats to 1.4-2.2 in dogs. The level of brain/blood ratio also appeared to impact adverse events with the most significant CNS adverse events including ataxia seen in the dog model. Blood-brain barrier permeability is generally not measured in clinical trials and the optimal animal model for extrapolating to humans is not clear, in our view. As such, we believe cautious dose escalation in Phase I is appropriate to fully assess potential CNS toxicity in human subjects.

Lastly, the compound has demonstrated strong preclinical tumor inhibition in a ROS1-driven Ba/F3 mouse xenograft model as highlighted in Table 8.

Table 8. RXDX-101 Active in ROS1+ Tumor Cell Line



Source: Company Documents (2013)

OVERVIEW OF TRK BIOLOGY – NEW TARGET FOR CANCER THERAPY

Trk gene rearrangements are believed to play a role in 1) central and peripheral neuronal cell development, 2) induction of growth arrest and 3) inhibition of programmed cell death. All variants retain five common thyrosine residues (Y670, Y674, Y490, Y675 and Y785) and all Trk receptors are activated by binding with neurotrophin nerve growth factors. Phosphorylation of the Y490 and Y785 residues is known to activate the RAS, PI3K and MAPK pathways that are well characterized in cancer tumor biology.

TrkA (tropomyosin receptor kinase A)/NTRK (neurotrophin tyrosine receptor kinase 1) is the best characterized gene variant in the family of tyrosine kinase receptors. The variant was first isolated in a human colon carcinoma cell line as a somatic rearrangement fusing TPM3 to the kinase domain of NTRK1. The binding domain was subsequently identified as nerve growth factor. TrkA, TrkB and TrkC are differentiated by different gene fusions with NTRK1 and have meaningfully different expression patterns in different solid tumor types.

Incidence of TrkA rearrangements varies by tumor type. Papillary thyroid cancer has among highest incidence of Trk rearrangements at about 12%, based on numerous studies published in literature. Other tumor types with elevated incidence include pancreatic cancer and glioblastoma. The incidence of Trk variants in NSCLC and colon cancer are around 2%. Overexpression of TrkB has been associated neuroblastoma and ovarian cancer.

The specific biologic impact of each Trk variant is different. Binding of TrkA with NGF has been shown to result in phosphorylation and dimerization of TrkA receptors. This activation of TrkA has been associated in upregulation of insulin-like growth factor-II (IGF-II) through the p53 and p73 pathways.

TrkB acts as an oncogene when overexpressed in the presence of its growth factor ligand, BDNF. This overexpression has been associated with expression of MYC and other oncogenes associated with cell growth and survival. As such, TrkB expression has been associated with aggressive disease and poor prognosis. The rationale and mechanism for directly regulating TrkB overexpression is still mixed, in our view.

Like TrkA, translocations of TrkC have been associated with a range of cancers including both hematologic and solid tumors. In the absence of the ligand, some studies suggest TrkC functions as a tumor suppressor gene. However, when TrkC binds with its ligand, NT-3, the kinase domain appears to upregulate signals for cell survival and cell proliferation. TrkC translocations have been associated with prostate cancer, breast cancer – including triple negative breast cancer – neuroblastoma and AML. More generally, the biology of TrkC suggests gene variants may be associated with increased risk of developing metastatic tumors.

OVERVIEW OF ROS1

Like ALK, ROS1 is part of the insulin-receptor superfamily. Dysregulation of the receptor is associated with proliferation and resistance to cell death. Over the past 2 years gene fusions and other variants in ROS1 have been identified in NSCLC patients. Patients with ROS1 alternations often respond to the ALK inhibitor crizotinib. Additionally, rearrangements of ROS1 have been identified in glioblastoma multiforme, colorectal cancer and other cancers. Prevalence of ROS1 variants is in low single digits. The binding ligand for the ROS1 receptor is currently unknown.

MEASURING ALK, ROS1 AND TRK VARIANTS

We view development of a companion diagnostic for RXDX-101 and other Trk inhibitors as a significant hurdle and potential rate limiting step for clinical trials. As a former diagnostic company, in our view, RXDX is uniquely positioned to address these challenges and plans to build an in-house CLIA certified laboratory to screen patients for late-stage clinical trials of RXDX-101. There are two classes of challenges in developing a companion diagnostic for RXDX-101, in our view: 1) technical and 2) regulatory.

As described above, the biology of TrkA, TrkB and Trk C is different and likely to require different diagnostic techniques to assess appropriate candidates for clinical trials. To the best of our knowledge there is no third party diagnostic testing laboratory currently offering testing for TrkA, TrkB and Trk C, in addition to ALK and ROS1 mutations. Additionally, scientific literature suggests there are both gene fusion variants of TrkA that can be detected with FISH assays and point mutations that are measured by PCR. The clinical significance of point mutations and potential benefit of RXDX-101 in patients with these point variants is unclear, in our view.

Our base case assumes RXDX uses off the shelf technologies for measuring ALK and ROS1 and collaborates with partners to validate technologies for measuring TrkA, TrkB and TrkC in its CLIA lab. Patients enrolled in clinical trials of the ALK inhibitor crizotinib were screened based on a FISH test from Abbott Labs that identifies ALK gene translocations. This is the only FDA-cleared companion diagnostic for crizotinib. Additionally, there are validated FISH tests for ROS1 and TrkA translocations available as laboratory developed tests.

While clinical experience with ALK testing suggests PCR tests may identify a larger patient population than FISH testing, there is limited data verifying whether the incremental patients achieve the same clinical response from targeted therapy. As such, we expect clinical development of RXDX-101 to focus on patient selection with FISH tests for ALK, ROS1 and potentially TrkA. If the drug wins regulatory clearance, we expect RXDX and clinicians to experiment with use of PCR testing.

This approach of combining existing technologies would likely require testing on FISH, IHC and potentially PCR platforms. While we view this testing algorithm to be feasible for clinical trials, we believe it may be challenging to transition to an FDA cleared IVD kit format. If the diagnostic is not widely available or impractical for community pathology labs and clinicians in developing economies, in our view, optimal access and commercial uptake of RXDX-101 may be challenging.

RXDX is developing an undisclosed methodology for evaluating most or all of the markers for RXDX-101 on a single technology platform. While we have not seen any technical specifications or training datasets for the in-house program and believe the program faces significant technical hurdles, we'd note that few biotechnology companies even have the capacity to explore development of proprietary diagnostic tests. While it may be too early to assess whether this in-house diagnostics expertise will bear fruit in development of RXDX-101, over time we expect RXDX's investment to yield dividends through the potential for accelerated time-to-market and potential for identifying a larger patient population of appropriate candidates for therapy.

Lastly, nearly all of FDA approved therapies with a companion diagnostic test are based on a single biomarker predicting response to a specific therapy. For RXDX-101, up to 5 different biomarkers may predict response to the drug. Whether interpreting the test will require a gene signature algorithm or will be based on a series of binary assessments is unclear. Given this relatively high level of regulatory complexity, in our view, maintaining full control of companion diagnostic development is a prudent investment for RXDX.

COMPETITIVE LANDSCAPE FOR TRK INHIBITORS

RXDX-101 is among the most advanced Trk inhibitors in either late-stage preclinical testing or Phase I clinical studies. As such, the general safety and efficacy profile of the class is not fully developed and assessing the optimal strategy for regulating TrkA, Trk B and TrkC in various tumor types is still in the exploratory stage. Importantly, companies are exploring development of molecules with different pan-kinase and single kinase targets, which, in our view, would be expected to generate different efficacy profiles in different patient populations. Identifying the correct patient population for each drug is a critical decision, in our view, and completing a Phase II program in a broad population of different tumor types is essential.

TSR-011

TSR-011 is arguably the closest direct competitor to RXDX-101. The drug is in Phase I/II development for solid tumor and hematologic malignancies with ALK or Trk A mutations. Data presented in 2013 at ESMO meeting suggest TSR-011 does have activity against TrkA and to a lesser extent TrkB and TrkC. While Tesaro does not describe TSR-101 as an inhibitor of ROS1, given the significant level of homology between ALK and ROS1, we would expect the drug to have at least some activity in ROS1+ tumors.

In September 2013 at the European Cancer Congress in Amsterdam, Tesaro presented interim Phase I data from TSR-011 in patients with ALK+ tumors including patients that had progressed following crizotinib. After 8 weeks of follow up, 65% of patients (11 of 17) had stable disease or partial response. Investigators observed no grade IV or grade V toxicity. A Phase IIa component of the study will evaluate efficacy in 1) ALK+ NSCLC patients not previously treated with crizotinib or other ALK inhibitors, 2) ALK+ NSCLC patients who progressed following previous treatment with an ALK inhibitor and 3) other solid tumors or lymphomas presenting with ALK or Trk mutations.

The primary potential weakness for TSR-011, in our view, is the Phase II design focused primarily on ALK+ NSCLC with limited exposure to other tumor types. As described below, the market for second-generation ALK inhibitors is crowded. We believe a strategy focusing on a subset of Trk+ patients (with and without ALK mutations) in NSCLC and other tumor types may be more constructive for pan-kinase inhibitors with activity against Trk.

PLX7486

PLX7486 targets the tyrosine kinase Fms along with TrkA, TrkB and TrkC. Plexxikon is enrolling a Phase I/II study. The Phase I component is a dose escalation study in patients with advanced solid tumors. The Phase II component will include two cohorts of PLX7486 in combination with gemcitabine and nab-paclitaxel. The Phase IIa study will enroll a range of patients with solid tumors and the Phase IIb study will enroll non-resectable pancreatic cancer patients. There is very limited data on the program available in the public domain.

LOXO-101

LOXO-101 is a Trk A/B/C inhibitor initially developed at Array Biopharma and licensed to Loxo Oncology in 2013. The drug does not target ALK, RET, ROS1 or other gene variants known to be associated with lung cancer. We believe LOXO-101 offers a significantly different clinical value proportion than RXDX-101 (i.e., maximum potency against a specific receptor vs pan-receptor inhibition). As such, we expect LOXO-101 to pursue a different development strategy with a focus on combination studies with other single-target tyrosine kinase inhibitors while we expect RXDX-101 to be used as a monotherapy or in combination with non-targeted therapies. While we see merit in the Loxo approach, we see potential challenges in enrolling clinical trials due to the relatively small number of Trk+ patients seen at most academic medical centers. The compound is entering Phase I/II in 2014.

ALK COMMERCIAL MARKET DYNAMICS

Variants of the insulin-receptor ALK (Anaplastic Lymphoma Kinase) are among the most widely characterized molecular targets for precision medicine. Following the introduction in 2011 of crizotinib for treatment of NSCLC patients with ALK variants, testing for variants in ALK became of standard of care in NSCLC staging. ALK variants have also been identified in diffuse large B-cell lymphoma, neuroblastomas and inflammatory myofibroblastic tumors. Prevalence is in the low-to-mid single digits.

While crizotinib has been shown an ORR of up to 61% in difficult to treat metastatic NSCLC cases, few patients experience a sustained durable response. Additionally, crizotinib does not penetrate the blood brain barrier and does not provide protection against brain metastasis (up to 50% of crizotinib-treated patients relapse with brain metastasis).

In response to these limitations several companies are developing second-generation ALK inhibitors that cross the blood-brain barrier and offer the promise of reducing brain metastasis. Some of the drugs such as LDK378 are optimized for ALK while others target ALK and one or more additional kinase targets including EGFR and Trk.

Finally, experience with crizotinib suggests new drug-resistant variants of ALK are likely to emerge over time, which suggests many ALK+ positive patients may receive multiple different ALK inhibitors over the course of disease progression.

LDK378

Novartis expects to complete 2 Phase II study of LDK378 in ALK+ NSCLC patients in 2014 with results supporting a potential regulatory filing in 2014. The drug has breakthrough therapy designation from FDA in crizotinib refractory ALK+ NSCLC patients.

At ASCO in 2013, Novartis presented data from 78 patients with ALK+ NSCLC. The 750mg demonstrated a 62% ORR in crizotinib naive patients and 59% in crizotinib refractory patients. Overall, the drug appears to have a comparable efficacy profile as crizotinib in treatment naïve patients (crizotinib was approved based on 2 studies with ORR of 50% and 61%, respectively), with impressive efficacy in refractory patients. LDK378 appears to be generally well tolerated with the primary concerns being gastrointestinal disturbance and transaminitis.

Based on this profile and time-to-market benefit conferred with breakthrough therapy status from FDA, we believe LDK378 is well positioned to become the first second-generation ALK inhibitor to reach the market. While the initial indication will be for patients refractory to crizotinib, we expect many oncologists – particularly in the U.S. – to use the product as frontline therapy for ALK+ positive NSCLC based on the broad efficacy profile and potential benefit in reducing brain metastases.

Alectinib (RO5424802/CH5424802)

Alectinib is an oral ALK inhibitor developed at Roche's Chugai division. Phase I/II results from a Japanese ALK-positive NSCLC study were published in the May 2013 issue of *The Lancet Oncology*. The Phase I cohort enrolled 24 patients while the Phase II component enrolled 46 patients at an optimal dose of 300 mg twice daily. Preliminary data presented at the ECC meeting in 2013 demonstrated an ORR of 59%. Data from the complete Phase II program is expected to support regulatory filing late in 2015.

AP-26113

AP-26113 was developed by Ariad and appears to be the most potent second-generation ALK inhibitor with additional activity against ROS1 and a range of EGFR variants. However, the drug demonstrated dose-dependent pulmonary adverse events in Phase I and Phase II studies. While AP-26113 did demonstrate a strong efficacy profile with 65% ORR in crizotinib refractory patients, in our view, the drug-specific pulmonary adverse event profile will limit its commercial profile.

UNCERTAIN ROLE FOR IMMUNOTHERAPY COMBINATION THERAPIES

Like many investors, we are upbeat regarding the potential of PD-1 inhibitors and other immunotherapies to changes in the clinical landscape of cancer treatment over the next 5 years. We believe immunotherapies offer a subset of patients an opportunity for more durable responses than have been seen previously with cytotoxic drugs and with targeted therapies.

However, many patients do not respond to immunotherapies and while the clinical responses tend to be more durable nearly all patients eventually relapse. As such, we do not see the total market opportunity for targeted therapies such as RXDX-101 declining significantly with the introduction of immunotherapies.

However, whether immunotherapies should be combined with targeted therapies in patients presenting with addressable mutations such as ALK, ROS1 and TrkA/B/C is an open question with limited data. Our base case and revenue model below assumes the therapies are used sequentially. If future clinical studies suggest using targeted therapy in combination with immunotherapies improves outcomes, there may be upside to our current forecast of the addressable market (i.e., patients might benefit from RXDX-101 in frontline combination therapy and as a monotherapy in second line or salvage therapy).

RXDX-101 REVENUE MODEL - $490M IN PEAK SALES

Our RXDX-101 revenue forecast focuses on NSCLC based on the large total patient population, known efficacy profile of ALK inhibitors and preclinical evidence of efficacy from Trk inhibition. While we believe there is a rationale for clinical utility in other solid tumors and potentially for hematologic malignancies such as AML, we do not include the potential sales in our revenue model. We will revisit this assumption following completion of a planned Phase II study of patients with various tumor types. Lastly, our model segments revenues by U.S. and ROW with U.S. market representing 90%+ of the market opportunity based on a clear regulatory and reimbursement path in the U.S. for targeted cancer therapies based on ORR.

About 225,000 Americans are diagnosed with lung cancer each year according to American Cancer Society. About 90% of these patients are diagnosed with NSCLC resulting in a screening population of about 200,000 cases each year. Various published studies suggest about 3%-6% of NSCLC patients have ALK mutations, 2%-4% have ROS1 mutations and 2%-4% have Trk mutations. In our revenue model we assume 4% of patients are ALK+, 2% ROS1+ and 2% Trk+ for an addressable U.S. population of around 16,000 patients. We'd note this addressable market is somewhat smaller than used by many drug companies developing targeted therapies. We believe the more conservative estimates are appropriate due to the challenge of driving compliance with diagnostic screening.

Our model calls for RXDX-101 to capture 25% of the addressable U.S. NSCLC market including majority market share in Trk+ patients. For international markets, we expect peak market share of 5%-7% based on limited uptake by patients with private health insurance and select national health plans.

We expect RXDX-101 to be priced at about $10,000 per one-month treatment cycle in the U.S. and $8,000 in other jurisdictions, which is similar to other frontline targeted cancer therapies. Our model assumes RXDX-101 is dosed continuously until disease progression. We believe a 50% improvement in PFS compared to the 7-8 months reported with crizotinib would be the minimum efficacy threshold to support commercialization. As such, we assume patients receive 11 monthly cycles of RXDX-101 for an average cost of $110,000 per patient in the U.S. and $88,000 in other markets.

We expect RXDX to eventually partner RXDX-101 for markets outside the U.S. After subtracting the undisclosed tiered royalty payable to Nerviano our estimate is 6% to 12%. We expect RXDX to receive a blended net royalty of 10% for commercial sales of RXDX-101 outside the U.S.

On net, our forecast translates to peak sales of $490M in 2022 including U.S. sales of $486M and international royalties of $4.3M (gross sales of $43M).

Table 9. RXDX-101 Revenue Model

RXDX-101 Revenue Model										
(in $millions)	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
U.S. ALK+ NSCLC Market Model										
Total Newly Diagnosed NSCLC Population										
Projected growth in NSCLC population	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%	0.7%
Projected Number of U.S. NSCLC Patients	199,386	200,782	202,187	203,602	205,028	206,463	207,908	209,363	210,829	212,305
% of U.S. NSCLC Patients ALK+	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%
% of U.S. NSCLC Patients ROS1+	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
% of U.S. NSCLC Patients Trk+	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
Target Population for RXDX-101 in NSCLC	15,951	16,063	16,175	16,288	16,402	16,517	16,633	16,749	16,866	16,984
% of Target NSCLC Population Receiving RXDX-101	0.0%	0.0%	0.0%	0.0%	0.0%	2.7%	10.9%	21.8%	25.0%	25.0%
Number of Patients Treated	0	0	0	0	0	448	1,809	3,643	4,217	4,246
Number of Scripts Per Patient	11	11	11	11	11	11	11	11	11	11
Total Number of Scripts Used Per Patient	0	0	0	0	0	4,928	19,897	40,072	46,382	46,707
Price Per Script	NA	NA	NA	NA	NA	$10,000	$10,100	$10,201	$10,303	$10,406
Increase in price per script	NA	NA	NA	NA	NA	2%	1%	1%	1%	1%
U.S. Sales of RXDX-101 ($M)	$0.0	$0.0	$0.0	$0.0	$0.0	$49.3	$201.0	$408.8	$477.9	$486.0
International Market Model										
Lung Cancer Population Outside the U.S.										
Projected growth in NSCLC population	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%	1.0%
Projected Number of non-U.S. NSCLC Patients	1,027,170	1,037,442	1,047,816	1,058,294	1,068,877	1,079,566	1,090,362	1,101,265	1,112,278	1,123,401
% of non-U.S. NSCLC Patients ALK+	4%	4%	4%	4%	4%	4%	4%	4%	4%	4%
% of non-U.S. NSCLC Patients ROS1+	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
% of non-U.S. NSCLC Patients Trk+	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
Target Population for RXDX-101 in NSCLC	82,174	82,995	83,825	84,664	85,510	86,365	87,229	88,101	88,982	89,872
% of Target NSCLC Population Receiving RXDX-101	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.0%	2.6%	4.2%	5.8%
Number of Patients Treated	0	0	0	0	0	0	894	2,291	3,737	5,213
Number of Scripts Per Patient	11	11	11	11	11	11	11	11	11	11
Total Number of Scripts Used Per Patient	0	0	0	0	0	0	9,835	25,197	41,110	57,338
Price Per Script	NA	NA	NA	NA	NA	NA	$8,000	$8,080	$8,161	$8,242
Increase in Price Per Script	NA	NA	NA	NA	NA	NA	1%	1%	1%	1%
Gross International Sales of RXDX-101 ($M)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$7.2	$18.5	$30.5	$43.0
Economics to RXDX	10%	10%	10%	10%	10%	10%	10%	10%	10%	10%
International RXDX-101 Revenue to RXDX	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.7**	**$1.9**	**$3.0**	**$4.3**
Worldwide RXDX-101 Revenue	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$0.0**	**$49.3**	**$201.7**	**$410.6**	**$480.9**	**$490.3**

Source: American Cancer Society and Ladenburg Thalmann estimates

PIPELINE DEVELOPMENT

While we expect most investors to focus primarily on the company's clinical-stage RXDX-101 program, in our view, the productivity of RXDX's in-house development platform will be a critical area of focus for creation of long-term shareholder value.

We believe RXDX has assembled an experienced management team with requisite pre-clinical development skills in medicinal chemistry, lead optimization and ADME/PK to efficiently advance the company's in-house drug development. Additionally, as highlighted in our investment thesis, we expect RXDX to look for select in-licensing opportunities from pharmaceutical companies. IND enabling studies for first of the in-house programs may be completed in 2015 or 2016 with the potential for a lead program to enter clinical development in 2016 or 2017, in our view. Management believes each of the three lead targets - Spark-1, Spark-2 and Spark-3 – are novel targets that are not currently being pursued by other commercial organizations. RXDX expects to focus solely on small molecule drug development.

Spark Programs – Novel Gene Signatures but Early in Development

RXDX's oncomethylome development engine has identified 6 novel epigenetic targets and is moving forward with 3 of them under the monikers SPARK 1-3. The oncomethylome database includes information on a range of genetic variants (sequence mutations, fusions, inversions, translocations and copy number variants) and epigenetic information. This data, which was culled primarily from publicly available databases, is combined with phenotypic information from the company's oncolome database.

Initial areas of focus are likely to include hypermethylation of CDK4 and synthetic lethality. The areas were chosen based on the demonstrated function of activated genes identified through a combination of whole genome sequencing with epigenome screening using a Miseq platform and microRNA expression profiles. These finding will be compared to the company's proprietary oncomethylome database of different populations. Based on these findings, RXDX hopes to develop a gene signature and the related diagnostic test.

We believe the last step - creation of the algorithm for a gene signature – is likely to be the most important in RXDX's development strategy and has the potential to be an important area of differentiation.

By way of example, TrkA was identified by the oncolome database as a potentially important target for proliferation and survival of solid tumors. Separately the target was validated by other academic and commercial organizations as a validated target for oncology drug development.

RXDX-102

RXDX-102 is a backup compound to RXDX-101 licensed from Nerviano. The compound was designed to provide broader pan-TRK inhibitor with better binding affinity for TrkB and TrkC. RXDX does not plan to invest in further development of RXDX-201 unless RXDX-101 demonstrates a drug-specific safety signal in clinical development.

COMMERCIAL PARTNERSHIPS

RXDX relies on partnerships for substantially all of its commercial supply chain and for pipeline expansion. While we believe this strategy contains certain risks in terms of insuring adequate commercial supply of product, in our view, it is appropriate for small molecule therapies such as RXDX-101 that do not have complex production requirements. The company currently controls global commercial rights to all of its pipelines programs. However, we expect RXDX to eventually seek commercial partners to sell RXDX-101 in Europe, Asia and other regions outside the U.S.

Nerviano

In October 2013, RXDX licensed global commercial rights to RXDX-101 and a backup compound, RXDX-102, from Nerviano Medical Sciences S.r.l The agreement calls for RXDX to fund all future clinical development expenses and pay a mid single-digit to low double-digit royalty on future sales of the two drugs. The company paid Nerviano $7M at closing and may be required to make up to $55M in future clinical and regulatory milestone payments. There are no sales-based milestones. We estimate that less than half the milestone payments are associated with clinical development with the remainder associated with global regulatory milestones. The first milestone payment is due upon initiation of a randomized Phase II study, which RXDX estimates could be in 2015. Total milestone payments for development of RXDX-102 are $50M. The company also agreed to pay Nerviano $1M by the end of 2014 for manufacturing and other technology transfer obligations.

SALES AND MARKETING

RXDX plans to develop a specialty sales force to promote RXDX-101 and other pipeline programs in the United States and seek commercial partners for geographies outside the U.S. We believe a field force of 60-90 people will be adequate to promote RXDX-101 in the U.S. for multiple solid tumor indications.

The commercial message for RXDX-101, in our view, is likely to be based on the superior efficacy a Trk-containing treatment modality, convenience of a single oral dose and potential first mover advantage in the market.

We expect the initial target market for RXDX-101 to be frontline use in ALK+ NSCLC and 2nd line therapy for patients that previously failed crizotinib. As mentioned above in our market model discussion, we expect second generation ALK inhibitors to replace crizotinib as frontline therapy in ALK+ NSCLC patients based on superior blood-brain barrier permeability and a related reduction in brain metastasis. We expect RXDX-101 to reach the market 18-24 months after the first next-generation ALK inhibitor, which may allow the product to benefit from growing clinician awareness of alternatives to crizotinib in frontline treatment of ALK+ NSCLC.

Our forecast assumes RXDX-101 is either the first or among the first Trk-directed therapies to reach the market. We'd note that other companies are pursuing different development strategies around Trk including stand-alone Trk inhibitors and other pan kinase inhibitor strategies. We expect RXDX to differentiate the profile of RXDX-101 based on dosing convenience of a single oral dose vs two or more drugs for stand-alone Trk inhibitors (i.e., separate pills or capsules for regulation of ALK and Trk).

As a potential first mover in Trk inhibition, we believe RXDX-101 is positioned to build a large database of patient data and clinician experience that should help to characterize the safety and efficacy profile of the drug before other products enter the market. We view this first mover advantage as a material barrier to commercial adoption for potential competitors.

Lastly, we expect safety to be an important consideration for clinicians as standard of care for targeted therapy moves toward regulation of multiple tyrosine kinase pathways. We believe it is too early to comment on the relative safety profile of RXDX-101 compared to other Trk inhibitors. However, we would note that published preliminary data for RXDX-101 and TSR-011 suggest a relatively benign safety profile for the class (no grade IV or grade V toxicities reported in either product's Phase I studies).

MANUFACTURING AND PRODUCTION

RXDX does not manufacture RXDX-101 and plans to rely on contract manufacturers and other third party manufacturers for API production and fill-finish on all pipeline programs.

The company received inventories of API drug product for RXDX-101 and RXDX-102 from Nerviano as part of licensing agreement, which, in our view, should be adequate to complete Phase I/II clinical trials. We expect RXDX to explore potential manufacturing process improvements for RXDX-101 and initiate production of another clinical trials lot of API before the end of 2014.

We expect RXDX to eventually transition from the facility used by Nerviano to a larger commercial contract manufacturing organization to support late-stage clinical trials and commercial supply of RXDX-101 and other products in its pipeline.

Given the company's current focus on small molecule drug candidates, we do not view manufacturing know how as an important point of differentiation and believe there may be multiple potential suppliers of raw material and manufacturing groups with requisite skills to support commercial scale up of RXDX-101.

TAXES

Based on its limiting operating history RXDX has accumulated limited deferred tax asset of about $553,000 as of December 31, 2012. In total, we expect the company to incur additional cumulative losses $120M-$150M to fund operations through to profitability (assuming 2018 launch of RXDX-101 and profitability in 2019). We expect substantially all of the tax assets associated with these operating losses to be available to offset future taxable income. Once tax assets are exhausted, we expect RXDX to pay an effective tax rate of 38% for federal and state income taxes.

IP

We believe RXDX has a strong intellectual property position including 2 issued U.S. composition of matter patents for RXDX-101 and RXDX-102 expiring in 2028 and 2027, respectively. The composition of matter patents are 8,299,057 and 8,114,865 for RXDX-101 and RXDX-102, respectively. There are issued composition of matter patents for RXDX-101 in New Zealand, South Africa and Ukraine and for RXDX-102 in Japan and Mexico. Composition of matter applications have been filed for both drugs in all major international markets.

Neither RXDX-101 nor RXDX-102 incorporates any technology sub-licenses or other intellectual property requiring royalties or license fees, according to RXDX management.

If RXDX is successful in moving any of its Spark programs into clinical development and commercialization, we believe these novel targets may enjoy significantly longer patent protection than RXDX-101 and RXDX-102. The company has rights to an additional nine pending U.S. patent applications and has filed or licensed rights to related patent applications in Europe and other large commercial markets outside the U.S. Many of the pending patent applications pertain to use of DNA methylation biomarkers and the company's methods for identifying new DNA methylation biomarkers.

SHAREHOLDER STRUCTURE AND TRADING PROFILE

Overall trading volume in the stock had been impacted by tight ownership structure with the top 3 holders controlling 37% of the outstanding shares prior the March 2014 underwritten equity offering. City Hill Venture Partners, an investment fund associated with CEO Jonathan Lim, controlled 13.9M shares outstanding (26% of pre-offering shares outstanding). City Hill Venture Partners and other insiders are subject to a 90-day lockup from completion of the March 2014 financing.

While we expect trading volumes to increase over the next 12-24 months as RXDX moves closer to generating proof-of-concept Phase II data for RXDX-101, the value of daily trading volumes may be constrained by the closely held ownership structure. Additionally, the ownership structure may impact future business development, M&A opportunities or other processes requiring shareholder approval.

Private Financing

Concurrent with the merger into a public shell in November 2013, all Ignyta series A preferred stock and series B preferred stock were converted into common stock. After adjusting for reverse stock splits and prior to financings associated with the reverse merger, employees and investors in the venture capital financings held 4,916,469 shares of common stock. Total invested capital in Ignyta prior to the reverse merger was $6M in equity from management and other private investors and $1.5M in venture loans. The equity was raised in venture rounds including $0.5M in a Series A round valued at $0.60 per share and $5.5M from a series B at $3.00 per share.

Shareholders from the publicly traded shell, Infinity Oil & Gas Co., received 87,336 shares of common stock in the post-merger company. A portion of shares held by Infinity Oil & Gas Co. shareholders were repurchased for cash resulting in a net total of 7,336 shares issued to Infinity Oil & Gas Co. shareholders. Concurrent with closing the merger Ignyta issued 7,740,142 shares of common stock to 52 accredited investors at $6.00 per share for gross proceeds of $47M. The company raised an additional $6.8M in December 2013 from the sale of 1,270,096 shares at $6.00 to 195 high net worth investors.

CAPITAL STRUCTURE

With completion of a $55.3M underwritten public offering in March 2014, RXDX has 20.0 million shares of common stock outstanding. About 4.9 million shares held by management and other insiders are subject to a lockup for 90 days from the March 19, 2014 closing date.

The company also has roughly 1.2 million outstanding employee stock options and a de minimis number of warrants that are excluded from shares outstanding. The average strike price on employee stock options is $4.33. Silicon Valley Bank has warrants to purchase 25,001 shares at a strike price of $3.00. Nerviano has warrants to acquire up to 16,667 shares at a strike price of $6.00 per share.

In conjunction with a $55.3M equity financing completed in March 2014, the company's common stock recently transitioned from the OTCQB Marketplace to the NASDAQ National Market under the ticker "RXDX". Prior to listing on NASDAQ the shares had limited blue sky registration in certain states.

In December 2013, the company expanded its credit agreement with Silicon Valley Bank from $1.5M to $10M. RXDX will pay interest only for the first 12 months followed by 36 equal monthly payments. The loan matures December 1, 2017 and carries an annual interest rate of 6.92%. The company will make a payment upon maturity of $1.05M or 10.5% of total principal amount.

MANAGEMENT

As of 2/28/14, RXDX employed 17 full-time employees including 12 in clinical development or research. While we expect RXDX to maintain a relatively small in-house development team, in our view, the company has secured experienced executives to lead each of the critical drug discovery and development positions. We expect the company to supplement this in-house capacity with contract service organizations. All employees are based at the company's office and laboratory facilities in San Diego.

Chief Executive Officer: Jonathan Lim is a co-founder and CEO of RXDX. Prior to forming RXDX, he helped create and fund several healthcare startups including Eclipse Therapeutics (a cancer stem cell spinout from Biogen), which was sold to Bionomics in 2012. Additionally, Lim served as President and CEO of Halozyme Therapeutics from 2003 through 2010. Under his leadership the company completed a successful public listing and signed several development partnerships with large pharmaceutical companies. Dr. Lim is a graduate of

Stanford University, received an M.D. from McGill University, and a M.P.H. from Harvard University, where he also completed an NIH Postdoctoral Fellowship.

Chief Financial Officer: Zachary Hornby joined RXDX in August 2012 as Chief Financial Officer and Vice President of Business Development. He has more than 12 years of senior biotechnology business development experience including positions as senior director of business development at Fate Therapeutics and director of Business Development of Halozyme Therapeutics. He has also held leadership roles with Neurocrine Biosciences and Transkaryotic Therapies. Mr. Hornby received B.S. and M.S. degrees from Stanford University and an M.B.A. from Harvard Business School.

Chief Medical Officer: Sara Zaknoen has a mix of commercial and academic experience in development of small molecule and cancer immunotherapies. Prior to joining RXDX in February 2014 as Chief Medical Officer, she was Chief Medical Officer at Polynoma where she oversaw the Phase III Melanoma Antigen Vaccine Immunotherapy Study. Previously, she served as Chief Medical Officer at Tragara Pharmaceuticals and at Cabrellis Pharmaceuticals. Zaknoen also worked at Novartis from September 2002 until September 2006 where she oversaw Phase II and Phase III studies for label expansion of Gleevec and registration studies for Tasigna. Additionally, Dr. Zaknoen served as Assistant Professor of Medicine at the University of Cincinnati Medical Center; Director of Experimental Therapeutics at the Western Pennsylvania Hospital, Western Pennsylvania Cancer Institute; and a Medical Staff Fellow at the National Cancer Institute. She received her M.D from the Indiana University School of Medicine.

Head of Medicinal Chemistry: Jean-Michel Vernier has more than 18 years of drug development experience with a focus of small molecule medicinal chemistry. Prior to joining the company in 2013, he was a co-founder and Vice President of Chemistry of targeted cancer therapy startup Selexagen Therapeutics. Previously, he was Vice President of Discovery Chemistry at Ardea Biosciences, which was sold to AstraZeneca in 2012. At Ardea he was responsible for leading the team that developed the MEK inhibitor RDEA119/BAY869766 and gout drug RDEA3170. He has also held senior chemistry positions at Merck and Valeant Pharmaceuticals. Dr. Vernier received a Ph.D. in synthetic organic chemistry from the University Louis Pasteur.

Head of Biology Research: David Anderson has more than 25 years of oncology and immunology drug development experience and is a co-founder of multiple biotechnology startups. He was a co-founder and CSO of diagnostic and immunology startup Proprius Pharmaceuticals (acquired by Cypress Bioscience in 2008 for $75M) and a co-founder and VP of Drug Discovery for Signal Pharmaceuticals (acquired by Celgene in 1999 for $275M). Following the acquisition of Signal he served as Chief Scientific Officer and Senior Vice President of Research for Celgene from 1999 through 2001. He has also served in senior drug development roles at Johnson & Johnson and Monsanto/GD Searle. He received a Ph.D. in Medical Microbiology and Immunology from the University of Missouri-Columbia.

Head of PK and Drug Metabolism: Paul Pearson is a former Global Head and Vice President Pharmacokinetics and Drug Metabolism at Amgen, former Executive Director of Preclinical Drug Metabolism at Merck Research Laboratories and former Director of Drug Metabolism at Pharmacia & Upjohn. His work contributed to development of oncology drugs Vectibix and Camptosar. He is also President of consultancy Pearson Pharma Partners and Editor of the Handbook of Drug Metabolism.

Head of Crystallography: Dave Matthews was a scientific founder of Agouron Pharmaceuticals, which was acquired by Pfizer. He spent nearly 20 years with Agouron/Pfizer where he was named Head of Structural Biology, Computational Chemistry and Bioinformatics. He is currently Adjunct Professor, Department of Molecular and Experimental Medicine, Division of Cellular Biology, The Scripps Research Institute. He was also a co-founder of Selexagen Therapeutics.

FINANCIAL MODELING ASSUMPTIONS

RXDX is a development stage company and is not likely to generate material commercial product revenues until 2018. As such, we do not view RXDX as an EPS-driven story and encourage investors to focus on clinical development and regulatory milestones as the primary avenues for creation of shareholder value.

We expect the cash burn rate to increase over the next several quarters as the company begins Phase II development for RXDX-101 in the United States. By our estimates, RXDX should burn $19.5M in 2014 and $25.3M in 2015. We estimate the company has a pro forma cash balance of $99.0M, which we believe is adequate to fund operations into 2017, excluding any potential impact from business development.

In terms of financial accounting, the company's merger into a public shell was treated as a reverse merger with historical balance sheet items and all future financial statements being those of the RXDX operating company.

Sales. We do not expect RXDX to recognize any revenues until the commercial launch of RXDX-101 in 2018. Our model assumes the company recognizes all RXDX-101 revenues in the U.S. and collects royalty revenue in other geographies.

COGS. While gross margin for small molecule therapeutics is typically 90%+, we expect reported gross margin to RXDX for RXDX-101 to be around 80% based on the structure of its agreement with Nerviano (tiered royalty of high single-digits to low-double digits).

G&A. As a private company RXDX enjoyed relatively low administrative costs of around $500,000 per quarter. With completion of the merger into a publicly traded shell in 4Q13, we expect administrative spending will triple to around $1.5M per quarter and increase 15%-20% annually over the next several years as RXDX continues to expand its management infrastructure to support additional business development activity.

Sales and Marketing. We do not expect RXDX to incur meaningful sales and marketing expense for RXDX-101 until 2018. We expect the company to hire 15-20 sales people to support launch of RXDX-101 and build a field sales force of about 90 people within 3 years of launch. In total, we expect peak sales and marketing expense for RXDX-101 to be $30M-$35M annually.

R&D. Given the transition of RXDX's business model from diagnostics to therapeutic development and licensing of RXDX-101 in 4Q13, historical financial statements provide little or no insight into future trends for R&D, in our view. Additionally, we expect the pace of investment in the company's in-house discovery based on the oncolome will be driven, at least in part, by access to capital. Our forecasted R&D spending of $14.3M and $20.0M for 2014 and 2015, respectively, assumes a base budget for preclinical development of $3M-$5M annually and an additional $2M annually for manufacturing and process development including assay development with the remainder related to clinical trials of RXDX-101.

EPS. We expect RXDX to record earnings per share of ($1.15) and ($1.38) for 2014 and 2015, respectively. We expect the company to achieve profitability in 2019.

Share Count. Following completion of two private placements in 4Q13 and an underwritten public offering in 1Q14, RXDX has 20.0 million shares outstanding and warrants and employee stock options convertible into up to 1.5 million shares.

PRIMARY RISKS

We think the primary risks of an investment in RXDX shares include, but are not limited to:

Clinical: While efficacy and safety of other ALK inhibitors for NSCLC has been well characterized in both clinical trials and commercial experience, there can be no assurance RXDX-101 will demonstrate clinically meaningful activity in NSCLC and other solid tumors. Additionally, RXDX-101 also inhibits ROS1 and TrkA/B/C. While there is a theoretical connection between inhibition of these tyrosine kinases and anti-tumor activity for a range of solid tumors including NSCLC, colon and glioblastoma, among others, there can be no assurances that future studies can be designed to evaluate the potential efficacy of co-inhibition of these tyrosine kinases or will confirm a positive impact on disease progression or survival, if a study is conducted. In the absence of clinical outcomes data, there can be no assurance that clinicians will accept or recognize the benefit of RXDX-101 over existing ALK inhibitors such as crizotinib. Additionally, the company is developing additional targeted cancer therapies based on its proprietary Oncolome database. There can be no assurance any future studies of pipeline programs will be adequate to support regulatory approval, reimbursement or commercial acceptance of pipeline programs. Lastly, RXDX relies on a virtual clinical development business model based on a small in-house management group and third party contractors. Loss of one or more executives could have an adverse impact of future clinical trials management.

Regulatory: RXDX is subject to oversight by multiple groups at the U.S. FDA including the Oncologic Drugs Advisory Committee for oncology drug development and Office of In Vitro Diagnostic Device Evaluation and Safety for companion diagnostics. There can be no assurance registration studies will be adequate to support regulatory filing with ODAC for RXDX-101 or any other pipeline product. Additionally, we expect the companion to diagnostic for RXDX-101 and other pipeline programs to be commercialized through diagnostic partners. There can be no assurance RXDX or its diagnostic partners will win timely PMA clearance for companion to RXDX-101 or any other pipeline product.

Competition: We are not aware of any other company developing a pan-inhibitor of ALK, ROS1 and TrkA/B/C. Additionally, there are currently no ROS1 or TrkA/B/C inhibitors approved for treatment of solid tumors in the U.S. or Europe. However, several companies have disclosed plans to develop therapies targeting TrkA/B/C. We believe RXDX-101 is currently the most advanced TrkA/B/C program in clinical development. There can be no assurance RXDX will be successful in maintaining its current leadership for timely commercialization of a TrkA/B/C inhibitor. Finally, several companies are developing second-generation ALK inhibitors with better blood-brain barrier than crizotinib. Some of these programs are more advanced than RGDX-101.

Financing: The company believes its financial resources will fund operations into at least 2017. However, depending on the pace of business development, RXDX may need additional capital to fund operations through Phase II proof-of-concept studies of RXDX-101. If Phase II studies are successful, RXDX may need access to additional capital through either internal sources or partnerships to fund registration studies and to fund commercialization. There can be no assurance RXDX will have access to capital in the future on adequate terms, or at all.

Partnership: RXDX will rely on partnerships with CROs, diagnostic product companies and other service providers to support clinical development and U.S. regulatory filings for RXDX-101 and its other pipeline programs. Additionally, we expect the company to seek commercial partners for RXDX-101 and its other pipeline programs in geographies outside the United States including Europe and Asia. There can be no assurance the partners will be successful in maintaining a steady supply of drug product, provide adequate support for clinical trials enrollment, optimize appropriate companion diagnostics or offer appropriate commercialization support in Europe, Asia and other regions outside the U.S. Lastly, the company licensed rights to RXDX-101 and RXDX-102 from Nerviano Medical Sciences.

While Nerviano is not responsible for conducting any future clinical development, the two companies have signed a service agreement for additional manufacturing and clinical support services through 2014. There can be no assurance Nerviano will provide adequate support for timely future development of RXDX-101.

Product Liability: Pharmaceutical companies may face potential product liability lawsuits associated with adverse events – both currently identified and identified through future clinical trials and commercial experience. Product liability claims may result in limiting future product promotion, removal of one or more products from the market and potential for financial penalties and fines that may adversely impact RXDX's cash flow and financial position, including cash balance and ability to meet various debt covenants.

Limited Operating History: While the company was formed in 2012, RXDX had limited operations as a drug development company prior to May 2013. This limited operating history may restrict the scope of information available for investors to form an investment opinion. RXDX is classified as an emerging growth company and is entitles to more limited disclosure requirements, which may make shares of RXDX less attractive to investors. The company went public in November 2013 through a reverse merger and trading volume in shares of RXDX has limited due in part to the small number of registered shares. There can be no assurance that there will be a liquid and orderly market for trading of RXDX shares in the near term, or ever. Additionally, if one or more holders of common stock covered by an effective registration statement seeks to sell stock, the share price may be adversely impacted.

Debt Repayment: The company has a $10M debt facility with Silicon Valley Bank Corp. that matures in December 2017. There can be no assurance RXDX will have adequate funds to repay the loan facility or that alternative debt financing will be available on acceptable terms, if at all.

Table 10. Ignyta Income Statement

Ignyta Income Statement												
(in $ millions)	**2013A**		**1Q14E**	**2Q14E**	**3Q14E**	**4Q14E**	**2014E**		**1Q15E**	**2Q15E**	**3Q15E**	**4Q15E**	**2015E**
Total product revenue	0.0		0.0	0.0	0.0	0.0	0.0		0.0	0.0	0.0	0.0	0.0
Other Revenue	0.0		0.0	0.0	0.0	0.0	0.0		0.0	0.0	0.0	0.0	0.0
Total Revenue	$0.0		$0.0	$0.0	$0.0	$0.0	$0.0		$0.0	$0.0	$0.0	$0.0	$0.0
COGS	0.0		0.0	0.0	0.0	0.0	0.0		0.0	0.0	0.0	0.0	0.0
Gross profit	$0.0		$0.0	$0.0	$0.0	$0.0	$0.0		$0.0	$0.0	$0.0	$0.0	$0.0
G&A	3.7		2.0	1.5	1.5	1.6	6.6		1.8	1.8	1.7	1.9	7.2
Research & development	3.2		3.0	3.3	4.0	4.0	14.3		4.7	4.9	5.2	5.2	20.0
Operating profit (loss)	($6.9)		(5.0)	(4.8)	(5.5)	(5.6)	($20.9)		(6.5)	(6.7)	(6.9)	(7.1)	($27.2)
Interest income	0.0		0.1	0.1	0.1	0.1	0.3		0.1	0.1	0.1	0.1	0.3
Interest expense	(0.2)		(0.2)	(0.2)	(0.2)	(0.2)	(0.7)		(0.2)	(0.2)	(0.2)	(0.2)	(0.7)
Other	(0.1)		0.0	0.0	0.0	0.0	0.0		0.0	0.0	0.0	0.0	0.0
Taxes	0.0		0.0	0.0	0.0	0.0	0.0		0.0	0.0	0.0	0.0	0.0
Net profit (loss)	(7.2)		(5.1)	(4.9)	(5.5)	(5.7)	(21.3)		(6.6)	(6.8)	(7.0)	(7.2)	(27.7)
Earnings (loss) per share from continuing ops	($1.94)		($0.37)	($0.24)	($0.28)	($0.29)	($1.15)		($0.33)	($0.34)	($0.35)	($0.36)	($1.38)
One-time gains (expenses)	($0.54)		$0.00	$0.00	$0.00	$0.00	$0.00		$0.00	$0.00	$0.00	$0.00	$0.00
Net income (loss) as reported	(14.2)		(5.1)	(4.9)	(5.5)	(5.7)	(21.3)		(6.6)	(6.8)	(7.0)	(7.2)	(27.7)
Earnings (loss) per share as reported	($3.83)		($0.37)	($0.24)	($0.28)	($0.29)	($1.15)		($0.33)	($0.34)	($0.35)	($0.36)	($1.38)
Weighted average common shares	3.7		13.9	20.0	20.0	20.0	18.5		20.0	20.0	20.0	20.0	20.0

Source: Company reports and Ladenburg Thalmann estimates

Table 11. Ignyta Pro Forma Balance Sheet

Ignyta Balance Sheet				
(in $ millions)	**3Q13A**	**4Q13A**		**1Q14E**
Assets				
Cash and short term investment	$2.5	$51.8		$99.0
Other	0.3	0.7		0.7
Total current assets	$2.8	$52.5		$99.6
Long-term investments	$0.0	$0.0		$0.0
Property & equipment	0.5	0.8		1.0
Total assets	$3.3	$53.3		$100.6
Liabilities				
Accounts payable	$0.4	$0.8		$1.5
Other accrued liabilities	0.2	0.7		0.7
Total current liabilities	$1.3	$1.5		$2.2
Long-term debt	$0.7	$9.0		$9.0
Other	0.1	1.1		1.1
Total liabilities	$2.1	$11.5		$12.2
Shareholder equity				
Paid-in capital	$5.5	$57.2		$108.5
Common stock	0.5	0.1		0.1
Accumulated deficit	(4.8)	(15.6)		(20.2)
Total shareholder equity	$1.2	$41.8		$88.5

Source: Company Reports

APPENDIX A: IMPORTANT RESEARCH DISCLOSURES

ANALYST CERTIFICATION

I, Kevin DeGeeter, attest that the views expressed in this research report accurately reflect my personal views about the subject security and issuer. Furthermore, no part of my compensation was, is, or will be directly or indirectly related to the specific recommendation or views expressed in this research report, provided, however, that:

The research analyst primarily responsible for the preparation of this research report has or will receive compensation based upon various factors, including the volume of trading at the firm in the subject security, as well as the firm's total revenues, a portion of which is generated by investment banking activities.

Additional information regarding the contents of this publication will be furnished upon request. Please contact Ladenburg Thalmann, Compliance Department, 570 Lexington Avenue, 11th floor, New York, New York 10022 (or call 212-409-2000) for any information regarding current disclosures, and where applicable, relevant price charts, in regard to companies that are the subject of this research report.

COMPANY BACKGROUND

Ignyta is developing personalized oncology drugs using diagnostic tests to identify patients most likely to respond to therapy. The company's lead product, RXDX-101, is a TrkA/B/C, ROS1, ALK inhibitor in Phase I development for the treatment of solid tumors. Ignyta hopes to move the program into Phase II development in 2015 for multiple indications including NSCLC. The San Diego-based company is also in pre-clinical development of other targeted cancer therapies based on its proprietary Oncolome molecular expression database.

VALUATION METHODOLOGY

Our $20.00 price target is based on a DCF analysis assuming 25% discount rate, 21.5 million shares on a fully diluted basis, terminal year (2022) FCF of $168M and 15% long term revenue growth rate.

RISKS

These risk factors (clinical, regulatory, competition, financing, partnership, product liability, limited operating history, and debt repayment) do not constitute all the potential risks of investing in the subject company's shares. Investors should refer to the company's SEC filings including the most recent forms 10-K and 10-Q for further details on the risks associated with an investment in the subject company's shares.

STOCK RATING DEFINITIONS

Buy: The stock's return is expected to exceed 12.5% over the next twelve months.
Neutral: The stock's return is expected to be plus or minus 12.5% over the next twelve months.
Sell: The stock's return is expected to be negative 12.5% or more over the next twelve months.

Investment Ratings are determined by the ranges described above at the time of initiation of coverage, a change in risk, or a change in target price. At other times, the expected returns may fall outside of these ranges because of price movement and/or volatility. Such interim deviations from specified ranges will be permitted but will become subject to review.

RATINGS DISPERSION AND BANKING RELATIONSHIPS (AS OF 02/28/14)

Buy:	77%	(46% are banking clients)
Neutral:	23%	(4% are banking clients)
Sell:	0%	(0% are banking clients)

BIOTECHNOLOGY STOCKS UNDER AUTHOR ANALYST COVERAGE ("The Universe")

ADMA Biologics (ADMA)

Aeolous Pharmaceuticals (AOLS)

Ignyta (RXDX)

Mesoblast (MBLTY)

Novavax (NVAX)

COMPANY SPECIFIC DISCLOSURES

Ladenburg Thalmann & Co. Inc. had an investment banking relationship with Ignyta (RXDX) in the past 12 months.

Ladenburg Thalmann & Co. Inc. makes a market in Ignyta (RXDX).

Ladenburg Thalmann & Co. Inc. received compensation for investment banking services from Ignyta (RXDX).

Ladenburg Thalmann & Co Inc. acted as placement agent and acted as Lead Manager in the Public Offering for Ignyta, Inc. (RXDX) in the past 12 months and received investment banking related compensation from Ignyta, Inc. (RXDX) in the past 12 months.

Ladenburg Thalmann & Co. Inc. intends to seek investment banking related compensation from Ignyta (RXDX) in the next 3 months.

OTHER COMPANIES MENTIONED: Amgen (AMGN, $122.93, Not Rated), Ariad Pharmaceuticals (ARIA, $7.84, Not Rated), Array Biopharma (ARRY, $5.18, Not Rated), AstraZeneca (AZN, $64.14, Not Rated), Biogen (BIIB, $318.53, Not Rated), Celgene (CELG, $144.40, Not Rated), Fate Therapeutics (FATE, $11.45, Not Rated), Johnson & Johnson (JNJ, $95.93, Not Rated), Merck & Co. (MRK, $54.66, Not Rated), Monsanto (MON, $113.28, Not Rated), Neurocrine Biosciences (NBIX, $16.47, Not Rated), Novartis (NVS, $81.73, Not Rated), Pfizer (PFE, $32.18, Not Rated), Roche Holding (RHHBY, $37.42, Not Rate), Tesaro (TSRO, $34.00, Not Rated) and Valeant Pharmaceuticals (VRX, $135.55, Buy Rated).

GENERAL DISCLAIMERS

Information and opinions presented in this report have been obtained or derived from sources believed by Ladenburg Thalmann & Co. Inc. to be reliable. The opinions, estimates and projections contained in this report are those of Ladenburg Thalmann as of the date of this report and are subject to change without notice. Any reference to the subject Company's or other third party website is provided for informational purposes only. Ladenburg Thalmann & Co. Inc does not endorse such websites and does not guarantee the accuracy of the content of those websites.

Ladenburg Thalmann & Co. Inc. accepts no liability for loss arising from the use of the material presented in this report, except that this exclusion of liability does not apply to the extent that such liability arises under specific statutes or regulations applicable to Ladenburg Thalmann & Co. Inc. This report is not to be relied upon in substitution for the exercise of independent judgment. Ladenburg Thalmann & Co. Inc. may have issued, and may in the future issue, other reports that are inconsistent with, and reach different conclusions from, the information presented in this report. Those reports reflect the different assumptions, views and analytical methods of the analysts who prepared them and Ladenburg Thalmann & Co. Inc. is under no obligation to ensure that such other reports are brought to the attention of any recipient of this report.

Some companies that Ladenburg Thalmann & Co. Inc. follows are emerging growth companies whose securities typically involve a higher degree of risk and more volatility than the securities of more established companies. The securities discussed in Ladenburg Thalmann & Co. Inc. research reports may not be suitable for some investors. Investors must make their own determination as to the appropriateness of an investment in any securities referred to herein, based on their specific investment objectives, financial status and risk tolerance.

Past performance should not be taken as an indication or guarantee of future performance, and no representation or warranty, express or implied, is made regarding future performance. The price, value of and income from any of the securities mentioned in this report can fall as well as rise. The value of securities is subject to exchange rate fluctuation that may have a positive or adverse effect on the price or income of such securities. Investors in securities such as ADRs, the values of which are influenced by currency volatility, effectively assume this risk. Securities recommended, offered or sold by Ladenburg Thalmann & Co. Inc. (1) are not insured by the Federal Deposit Insurance Company; (2) are not deposits or other obligations of any insured depository institution; and (3) are subject to investment risks, including the possible loss of some or all of principal invested. Indeed, in the case of some investments, the potential losses may exceed the amount of initial investment and, in such circumstances; you may be required to pay more money to support these losses.

The information and material presented in this report are provided to you for information purposes only and are not to be used or considered as an offer or the solicitation of an offer to sell or to buy any securities mentioned herein. This