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Biotechnology
Company Update
September 29, 2014
BUY
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IGNYTA, INC.

RXDX-101 Shows Strong Safety and Efficacy in Two New Dosing Regimens

RXDX (NASDAQ)

Company & Market Data	
Closing Price (as of 09/26/2014):	$7.54
Rating:	BUY
Price Target:	$20.00
52 Week Range:	$1.00 - $20.00
Shares Outstanding (MM):	20
Market Capitalization (MM):	$148
Cash (MM):	$95.1
Debt (MM):	$9.1
Fiscal Year End:	Dec

Estimates			
EPS	**2013A**	**2014E**	**2015E**
1Q	—	$(0.28)A	$(0.34)
2Q	—	$(0.28)A	$(0.36)
3Q	—	$(0.48)	$(0.38)
4Q	—	$(0.31)	$(0.39)
Full Year	$(1.94)	$(1.36)	$(1.47)
Revenue (MM)	$0.0	$0.2	$0.0

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 proprietary Oncolome molecular expression database.

Highlights

On 9/28/14 at the ESMO meeting, RXDX presented a positive update for RXDX-101 including preliminary data on two new dosing regimens -- 200MG/M2 daily and 400Mg/M2 for 4 days on and 3 days off continuous weekly dosing. Neither of these new cohorts were described in an abstract released earlier this month. Importantly, data from the new dosing cohorts did not identify any unexpected toxicities and reaffirmed the activity of RXDX-101 in a range of tumor histologies. While the follow up for the 2 new continuous dosing cohorts was limited - total of 6 patients dosed; all completed at least 1 cycle - we view the continued absence of Grade 3 toxicity including neurotoxicity as an important finding (i.e., RXDX-101 crosses the blood-brain barrier and potential signals for ataxia were seen in dog models). Finally, we note that RXDX-101 demonstrated strong efficacy in ROS1 variants, which may offer an accelerated path to market. Reiterate Buy rating and $20.00 PT.

- **What's New?** RXDX announced data from 3 Phase I studies at ESMO: 3 patients dosed at 200MG/M2 daily, 3 patients dosed at 400MG/M2 for 4 days on and 3 days off of continuous weekly dosing, and an update on 6 patients dosed for 4 days on and 3 days off for 3 weeks of a 4 week cycle. 2 of 3 patients in the 400Mg/M2 cohort had a clinical response including 1 complete response in a ROS1 NSCLC patient. As a reminder, at ASCO in June data was presented demonstrating 6 of 19 patients from the first Phase I study had a clinical response (4 PRs and 2 stable disease) and were still receiving RXDX-101 including one colorectal cancer patient with a confirmed TrkA mutation. The TrkA responder progressed after 4 cycles due to a metastatic adrenal gland tumor (TrkA+ colorectal tumor did not show signs of progression). Given the rapid signs of clinical response in a patient with extremely advanced disease, we believe RXDX-101 has demonstrated clear signs of clinical efficacy against TrkA and continue to believe RXDX-101 is among the most advanced therapies targeting TrkA/B/C. Additionally, there were no new Grade 3 or Grade 4 toxicities reported at ESMO. Additional details on Page 2.
- **NEJM ROS1 Data Points to Accelerated Path to Market:** We believe RXDX-101's strong activity in patients with a ROS1 variant (1 CR and 2 PRs in 4 patients) is an important finding in light of data from a separate study of crizotinib published this weekend in the New England Journal of Medicine (NEJM). The NEJM study found crizotinib, which is approved for ALK+ NSCLC, demonstrated a 72% response rate in 50 patients with ROS1 NSCLC variants. We remind investors that several of the 2nd-generation ALK inhibitors were optimized for ALK binding and appear to have lower binding affinity for ROS1 than crizotinib. RXDX-101 was developed within a Pfizer (PFE, $29.72, Not Rated) laboratory as a potential replacement for crizotinib and demonstrated stronger binding affinity for ROS1 than crizotinib in preclinical models. We believe this combination of 1) strong clinical response against ROS1 in Phase 1 studies, 2) proof of concept for the role of ROS1 in a large NSCLC crizotinib study, and 3) strong binding affinity in preclinical studies suggest ROS1 NSCLC may offer an accelerated path to market for RXDX-101. If approved for ROS1 NSCLC, we believe RXDX-101 may be preferred by many clinicians based on capacity to cross the blood-brain barrier and prevent brain metastases.

Background on ALKA-372-001 Study Design

The protocol, which was drafted by partner Nerviano, 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. The study dosed patients at 100mg/m2, 200mg/m2, 400mg/m2, 800mg/m2, 1200mg/m2 and the maximum dose of 1600mg/m2 twice daily. The protocol allowed for intrapatient up-titration of dose. 20 patients were enrolled and 19 completed dosing (one could not tolerate capsule burden).

Investigators presented data at ASCO in an oral abstract. The study dosed 12 NSCLC, 3 neuroblastoma, 2 colorectal cancer, 1 pancreatic cancer and 1 Leiomyosarcoma. A total of 6 of 19 patients that completed dosing had a clinical response (4 PRs and 2 stable disease) compared to 2 patients described in the abstract (1 PR and 1 stable disease). Excluding 3 patients treated at 100mg/m2 (sub-therapeutic dose) and 3 patients with point mutations (typically less likely to respond to tyrosine kinase inhibitors than gene rearrangements), there were 13 patients that received both therapeutic doses and had clinically actionable mutations for an implied overall response rate of 46%. Responders included 1) an ALK+ neuroblastoma patients with PR at 16 cycles, 2) ALK+ NSCLC patient with stable disease at 14 cycles, 3) ROS1+ pancreatic patient with stable disease through 11 cycles, 4) ALK+ NSCLC (intolerant to crizotinib) with a PR through 6 cycles, 5) ROS1+ NSCLC patient with PR through 5 cycles and 6) TrkA+ colorectal cancer patient with PR after 2 cycles. All patients received between 800mg/m2 and 1200mg/m2.

PK analysis indicates maximum concentrations of RXDX-101 were generally achieved within 2 to 4 hours of administration with dose escalating concentrations up to 800 mg/m2. The mean terminal half-life was 21 to 32 hours and steady state was reached within 4 days.

Table 1.

Ignyta Income Statement												
(in $ millions)	2013A		1Q14A	2Q14A	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	0.2	0.0	0.0	0.2		0.0	0.0	0.0	0.0	0.0
Total Revenue	$0.0		$0.0	$0.2	$0.0	$0.0	$0.2		$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	$0.2	$0.0	$0.0	$0.2		$0.0	$0.0	$0.0	$0.0	$0.0
G&A	3.7		1.8	2.0	1.7	1.9	7.4		1.9	2.1	2.0	2.2	8.3
Research & development	3.2		2.2	3.6	7.5	4.0	17.3		4.7	4.9	5.2	5.2	20.0
Operating profit (loss)	($6.9)		(3.9)	(5.5)	(9.2)	(5.9)	($24.5)		(6.6)	(7.0)	(7.2)	(7.4)	($28.3)
Interest income	0.0		0.0	0.1	0.1	0.1	0.2		0.1	0.1	0.0	0.0	0.2
Interest expense	(0.2)		(0.1)	0.0	(0.2)	(0.2)	(0.5)		(0.2)	(0.2)	(0.2)	(0.2)	(0.7)
Other	(0.1)		(0.0)	(0.0)	0.0	0.0	(0.1)		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)		(4.1)	(5.4)	(9.3)	(6.0)	(24.8)		(6.8)	(7.1)	(7.4)	(7.6)	(28.8)
Earnings (loss) per share from continuing ops	($1.94)		($0.28)	($0.28)	($0.48)	($0.31)	($1.36)		($0.34)	($0.36)	($0.38)	($0.39)	($1.47)
One-time gains (expenses)	($0.57)		$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)		(4.1)	(5.4)	(9.3)	(6.0)	(24.8)		(6.8)	(7.1)	(7.4)	(7.6)	(28.8)
Earnings (loss) per share as reported	($3.83)		($0.28)	($0.28)	($0.48)	($0.31)	($1.36)		($0.34)	($0.36)	($0.38)	($0.39)	($1.47)
Weighted average common shares	3.7		14.5	19.6	19.6	19.6	18.3		19.6	19.6	19.6	19.6	19.6

Source: Company reports and Ladenburg Thalmann estimates

Company and Industry-Specific 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 and acquired drug candidates including RXDX-103 and RXDX-104. 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.

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.

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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 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 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 (September 29, 2014)

Rating	%	IB %
BUY	74.2	60.6
NEUTRAL	25.8	38.9
SELL	0.0	0.0

COMPANIES UNDER KEVIN'S COVERAGE

ADMA Biologics, Inc. (ADMA)
BG Medicine, Inc. (BGMD)
diaDexus, Inc. (DDXS)
Genetic Technologies, Ltd. (GENE)
Mesoblast Ltd. (MBLTY)
Navidea Biopharmaceuticals Inc. (NAVB)
Opko Health, Inc. (OPK)
Ignyta, Inc. (RXDX)
Aeolus Pharmaceuticals Inc. (AOLS)
CombiMatrix Corporation (CBMX)
Exact Sciences Corp. (EXAS)
Genomic Health Inc. (GHDX)
Myriad Genetics Inc. (MYGN)
Novavax, Inc. (NVAX)
Parnell Pharmaceuticals Holdings LTD (PARN)
Sequenom Inc. (SQNM)

COMPANY SPECIFIC DISCLOSURES

Ladenburg Thalmann & Co. Inc. makes a market in Ignyta, Inc..

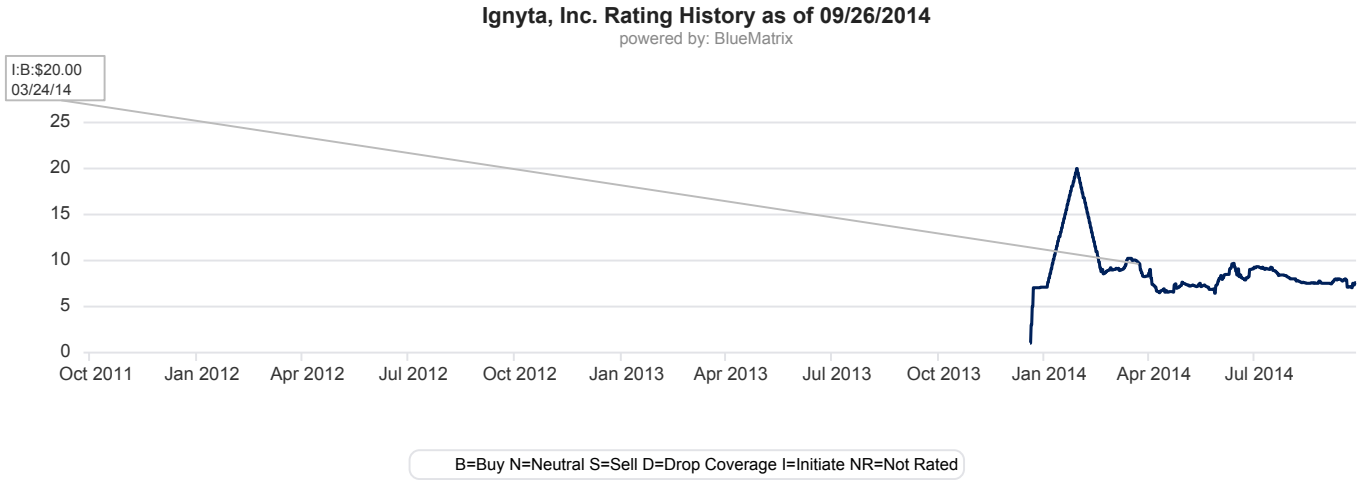
Ladenburg Thalmann & Co. Inc. has managed or co-managed a public offering for Ignyta, Inc. within the past 12 months.

Ladenburg Thalmann & Co. Inc. intends to seek compensation for investment banking and/or advisory services from Ignyta, Inc. within the next 3 months.

Ladenburg Thalmann & Co. Inc received compensation for investment banking services from Ignyta, Inc. within the past 12 months.

Ladenburg Thalmann & Co. Inc had an investment banking relationship with the Ignyta, Inc. within the last 12 months.

INVESTMENT RATING AND PRICE TARGET HISTORY



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