

Reason for report:

COMPANY UPDATE

IGNYTA, INC.

Investor Day Highlights Lead Position in Trk

• **Bottom Line:** At the RXDX investor day, key opinion leaders in the Trk field and targeted therapy provided their insights and we walked away more positive on the competitive position for RXDX-101. One KOL considered '101 as the most potent Trk inhibitor among 12 compounds he has tested. Although all Trk inhibitors are in early stage with no clear winner, we believe '101 has the most compelling body of clinical data following recent update at ESMO ([LINK](#)), which continues to support '101 lead development stage in Trk targeted therapy. In addition to Trk rearrangement, KOLs highlighted additional evidence of TrkB overexpression where clinical implication should provide upside market potential for Trk targeted therapy. Beyond Trk, the KOL was excited about differentiated activity against RET from the early asset '104 (see our prior note [LINK](#)). We reiterate OP rating and \$14 valuation for RXDX.

• **RXDX-101 is considered as the most potent Trk inhibitor by a KOL.** Dr. Garrett Brodeur from University of Pennsylvania has first hand experience with 12 Trk inhibitors from 8 companies, including Phase I trial with lestaurtinib (from Cephalon/TEVA) where initial activity was seen in neuroblastoma patients (*Minturn et al, Cancer Chemother Pharmacol, 2011, 68:1057*). In his view, '101 is the most potent Trk inhibitor among 12 tested compounds, supported by in vitro data as well as data from a SY5Y-TrkB mouse model where '101 showed better event free survival rate vs. lestaurtinib. These data support future drug development for '101 in neuroblastomas where TrkB/BDNF (brain derived neurotrophic factor) overexpression occurs in 50-60% of high-risk neuroblastoma.

• **Beyond Trk rearrangement, Trk over expression could provide significant upside to market potential.** While the current focus is still on Trk rearrangement where diagnostics and clinical development is relatively straightforward, Trk over expression could represent a large market potential for '101. Although the high-risk neuroblastoma market is small, positive read through to other indications (such as triple negative breast cancer) could reach \$1B market potential.

• **Good blood brain barrier penetration and clean safety data so far are favorable to '101.** The good BBB penetration from animal studies appears favorable for '101 in lung cancers where high percentage of patients developed brain metastasis. Although there was a concern on ataxia (seen in animal, likely through targeting TrkB/BDNF in brain), both KOLs view human data very clean from several dosing regimens, which could serve as backup dosing regimens if severe toxicity emerges in the continuous dosing regimen.

• **Multiple targets are an advantage for '101, according to KOL.** Although some arguments were raised where high selectivity should result in better safety profile and capability of dosing higher, Dr. Alexander Drilon from Memorial Sloan Kettering Cancer Center noted that high potency against Trk, ALK, and ROS1 multiple targets provides additional therapeutic indications for '101 without obvious on-target toxicity.

Key Stats:

(NASDAQ:RXDX)

S&P 600 Health Care Index:	1,271.11
Price:	\$6.74
Price Target:	\$14.00
Methodology:	Probability-weighted DCF analysis, 10% discount rate
52 Week High:	\$20.00
52 Week Low:	\$1.00
Shares Outstanding (mil):	19.6
Market Capitalization (mil):	\$132.1
Book Value/Share:	\$5.37
Cash Per Share:	\$5.13
Dividend (ann):	\$0.00
Dividend Yield:	0.0%

Book Value: Pro Forma

Cash Per Share: Pro Forma



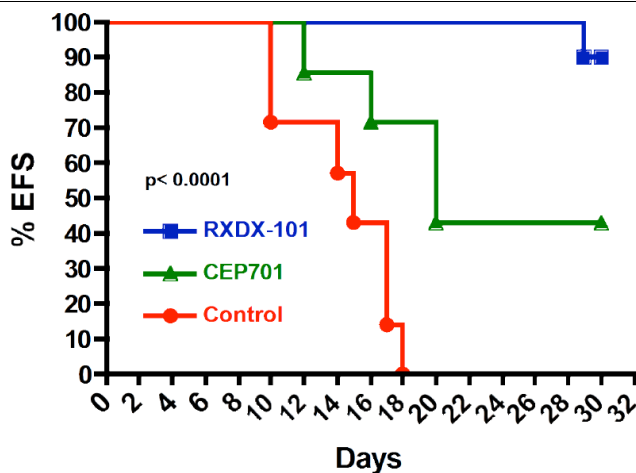
Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2013A	--	--	--	--	0.0	--	--	--	--	(\$3.83)	NM
2014E	0.0A	0.0	0.0	0.0	0.0	(\$0.28)A	(\$0.26)	(\$0.37)	(\$0.41)	(\$1.35)	NM
2015E	--	--	--	--	0.0	--	--	--	--	(\$1.81)	NM

Source: Company Information and Leerink Partners LLC Research

INVESTMENT THESIS

RXDX is a biotech company with a focus on targeted therapies and molecular diagnosis in oncology. RXDX's approach of targeting molecular oncogenic drivers has historically resulted in highly effective agents. Despite low incidence of many genetic alterations including Trk and ROS1 rearrangement, molecular screening started to become a standard practice in NSCLC where oncogenic driver mutations have been identified in ~70% of adenocarcinoma patients. Clinical successes with EGFR, ALK, ROS1, HER2, BRAF inhibitors have shown high efficacy in several cancer types. Although RXDX's lead candidate RXDX-101 (oral pan-Trk, ROS1 and ALK inhibitor) is still in early stage clinical development, we believe historical precedence suggests a higher-than-average chance of success in identifying highly effective agents which we believe is increasingly the direction for the development of new cancer therapies. We believe the main value for RXDX-101 lies in the market potential for cancers with Trk genetic alteration, an emerging target for NSCLC. Although many compounds have activity against Trk, so far, only a handful of companies have focused clinical programs targeting Trk, whereas RXDX has dedicated effort to target Trk in multiple tumor type with the potential to develop a first-in-class Trk inhibitor. Although still early with limited clinical data, observed ALK activity and initial Trk activity (seen in one patient) bode well for RXDX-101 as a Trk inhibitor, where in vitro activity is ~10X more potent vs. ROS1 and ALK. The new global Phase I study with modified continuous dosing schedule could provide insight on safety and clinical activity. Recent licensing deal with Nerviano further expand the pipeline targeting Cdc7 (cell cycle kinase inhibitor) and RET (tyrosine kinase inhibitor). Additionally, Technology platform and integrated Rx/Dx strategy with genomic and epigenomic mining of oncolome provide potentially six targeted therapies with companion diagnostics in 2015 and beyond.

RXDX-101 Increases Event Free Survival in SY5Y-TrkB Nude Mouse Model



Source: Company Reports

RXDX – Upcoming Events

Timing	Event
RXDX-101 (Pan-Trk, ROS1, ALK inhibitor)	
4Q:14	Ongoing STARTRK-1 Phase I/II dose escalation study with continuous dosing
	Basket Trial expansion cohorts in TrkA, TrkB, TrkC, ROS1, ALK
ASCO 2015	STARTRK data
RXDX-103 (Cdc7 inhibitor)	
Early '16	Initiating Phase I study
RXDX-104 (RET inhibitor)	
2015	Define a candidate
2016	Initiating Phase I study
Spark-1 (Rx/Dx novel target)	
2015	IND candidate

Source: Company Reports

RXDX – Pipeline

Stage of Development	Current Status/Upcoming Developments
RXDX-101 (Pan-Trk, ROS1, ALK inhibitor)	
Phase I	Phase I dose escalation study of intermittent dosing in Italy with 20-30 pts in each of ALK, ROS1 or TrkA alterations.
STARTRK-1	Global Phase I/II dose escalation study in US, EU and Asia with continuous dosing in 6-24 pts with Trk, ROS, or ALK alterations initiated in July, '14
	Basket trial expansion cohorts at RP2D with 15-20 pts in each cohort with TrkA, TrkB, TrkC, ROS1 or ALK alterations
STARTRK-2	Pivotal registration trials in most promising tumor types and targets based on ORR and other clinical observations
RXDX-102 (Pan-Trk inhibitor)	
Preclinical	Back-up to RXDX-101
RXDX-103 (Cdc7 inhibitor)	
Preclinical	Enter clinical in 2016
RXDX-104 (RET inhibitor)	
Preclinical	Define candidate in 2015, enter clinical in 2016
Spark-1 Rx/Dx program	
Discovery	IND candidate in 2015
Spark-2 Rx/Dx program	
Discovery	
Spark-3 Rx/Dx program	
Discovery	

Source: Company Reports

VALUATION

Our \$14 price target is derived from a probability-weighted DCF analysis. We project US launch for RXDX-101 in NSCLC (both ROS1+ and TrkA re-arrangement, 50% probability) in 2018, and EU launch in 2019. We assume full internal commercialization in both the US and EU with 8% sales royalty to Nerviano. We include \$100M cash in 1Q:14 following recent IPO and assign \$40M valuation to pipeline. We assign no terminal value to RXDX-101. We believe 10% discount rate is appropriate given probability-weighted sales estimates.

RISK TO VALUATION

- RXDX-101 is at early stage with limited clinical efficacy data in patients with ROS1 and ALK genetic alteration.
- Although some preclinical data showed RXDX-101 activity against crizotinib resistant cell lines, activity in crizotinib resistant patients is still unknown.
- New toxicity may emerge under the modified continuous dosing regimen in STARTRK Phase I/IIa study.
- Underlying market opportunity for Trk remains to be clarified.
- Competitive landscape remains widely open and other competitors could emerge rapidly.
- Even with good efficacy as a monotherapy, RXDX-101 may need to be combined with other agents to be competitive.
- Financing risk – Current cash only support operation into 2016 and RXDX will require additional capital raise before turning to profitability.

RXDX - Income Statement (\$000, except per share value)	2012A	2013A	Mar-14A	Jun-14E	Sep-14E	Dec-14E	2014E	2015E	2016E	2017E	2018E	2019E
RXDX-101 sales - US							0	0	0	0	8,471	58,747
% to RXDX							92%	92%	92%	92%	92%	92%
RXDX-101 sales - Ex-US							0	0	0	0	0	21,173
% to RXDX							92%	92%	92%	92%	92%	92%
Total revenue	0	0	0	0	0	0	0	0	0	0	7,793	73,526
COGS	0	0	0	0	0	0	0	0	0	0	678	6,394
R&D	708	10,171	2,183	3,056	4,584	5,272	15,095	30,274	43,897	54,871	54,871	53,225
SG&A	548	3,731	1,756	2,107	2,739	3,013	9,616	15,383	16,921	33,843	50,764	55,841
Total expenses	1,256	13,902	3,939	5,163	7,324	8,285	24,711	45,657	60,818	88,714	106,313	115,459
Operating Income	(1,256)	(13,902)	(3,939)	(5,163)	(7,324)	(8,285)	(24,711)	(45,657)	(60,818)	(88,714)	(98,520)	(41,933)
Other income (expenses)	0	(106)	(163)	0	0	0	(163)	0	0	0	0	0
Interest income (expenses)	(23)	(204)										
Tax	1	2	5	0	0	0	5	0				
Net income to common shares	(1,280)	(14,214)	(4,107)	(5,163)	(7,324)	(8,285)	(24,879)	(45,657)	(60,818)	(88,714)	(98,520)	(41,933)
EPS - basic	(2.00)	(3.83)	(0.28)	(0.26)	(0.37)	(0.41)	(1.35)	(1.81)	(2.00)	(2.19)	(2.03)	(0.86)
EPS - dilutive	(2.00)	(3.83)	(0.28)	(0.26)	(0.37)	(0.41)	(1.35)	(1.81)	(2.00)	(2.19)	(2.03)	(0.86)
Basic shares	640	3,712	14,501	19,580	19,775	19,973	18,457	25,237	30,456	40,486	48,527	48,576
Dilutive shares	640	3,712	16,186	21,268	21,467	21,668	20,147	26,940	32,167	42,199	50,241	50,291

Sources: Company Reports, Leerink Partners

Disclosures Appendix

Analyst Certification

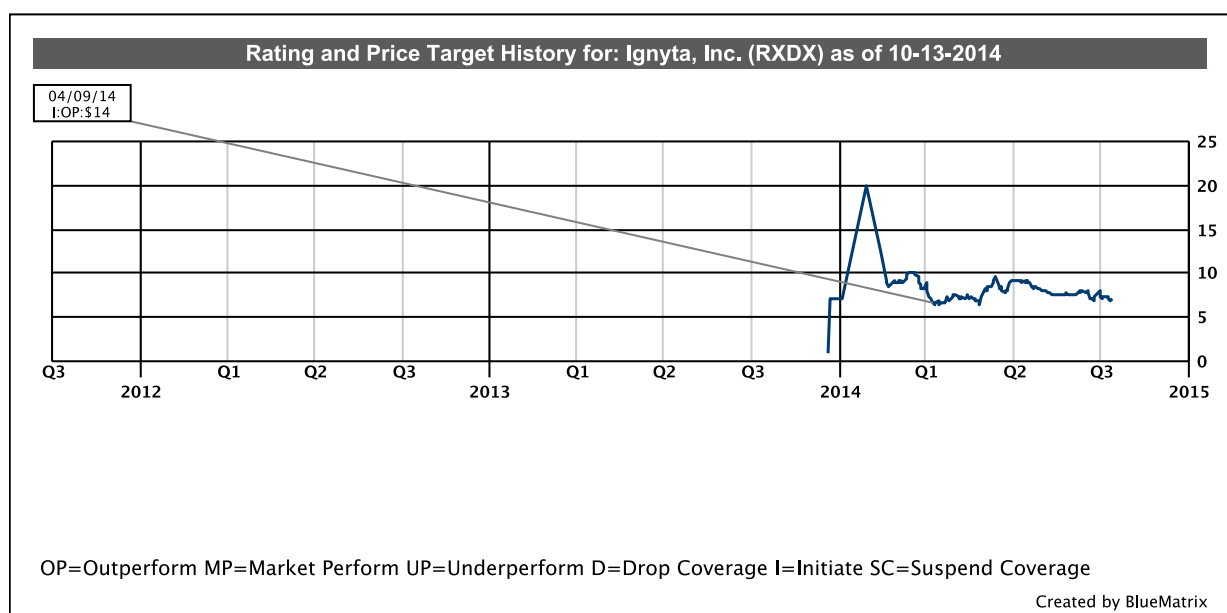
I, Gena Wang, Ph.D., CFA, certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

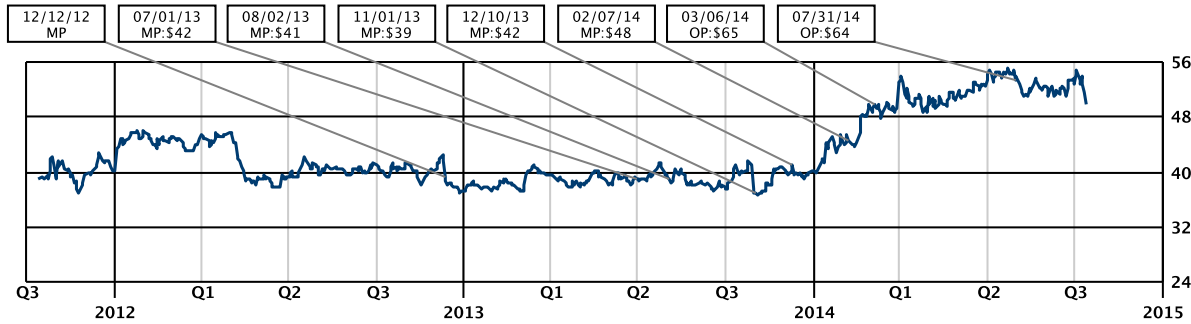
Valuation

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Rating and Price Target History for: Teva Pharmaceutical Industries Ltd. (TEVA) as of 10-13-2014


Leerink Swann initiated coverage of TEVA with an Outperform rating on August 18, 2011. On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

Created by BlueMatrix

Distribution of Ratings/Investment Banking Services (IB) as of 09/30/14				
Rating	Count	Percent	IB Serv./Past 12 Mos.	
			Count	Percent
BUY [OP]	138	69.30	51	37.00
HOLD [MP]	61	30.70	2	3.30
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

Outperform (Buy): We expect this stock to outperform its benchmark over the next 12 months.

Market Perform (Hold/Neutral): We expect this stock to perform in line with its benchmark over the next 12 months.

Underperform (Sell): We expect this stock to underperform its benchmark over the next 12 months. The degree of outperformance or underperformance required to warrant an Outperform or an Underperform rating should be commensurate with the risk profile of the company.

For the purposes of these definitions the relevant benchmark will be the S&P 600® Health Care Index for issuers with a market capitalization of less than \$2 billion and the S&P 500® Health Care Index for issuers with a market capitalization over \$2 billion.

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In the past 12 months, the Firm has received compensation for providing investment banking services to Ignyta, Inc. .

Leerink Partners LLC makes a market in Ignyta, Inc. and Teva Pharmaceutical Industries Ltd.

Leerink Partners LLC has acted as the manager for a public offering of Ignyta, Inc. in the past 12 months.

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