April 9, 2014

OUTPERFORM

Reason for report:

INITIATION

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IGNYTA, INC.

Novel Targeted Therapy with Potential 1st Mover Advantage; Initiating with OP

• **Bottom Line:** We are initiating coverage on RXDX with an Outperform rating and $14 valuation. Given many historical precedents, we see RXDX's targeted therapy in oncology has a better than average chance of success despite that the lead compound RXDX-101 is still in early stage development. Additionally, focusing on newly emerged Trk oncogenic driver may provide first-mover advantage in targeted therapy in NSCLC.

• **Trk is an emerging oncogenic target and RXDX has potential 1st mover advantage.** We think value for RXDX-101 lies in the market potential for pan-Trk cancers. TrkA rearrangement as an oncogenic driver has emerged following breakthrough discovery (2013). Many compounds have activity against Trk, but only a few companies have dedicated clinical programs targeting Trk. RXDX has the potential to develop a 1st-in-class Trk inhibitor targeting a ~$1-2B US market opportunity.

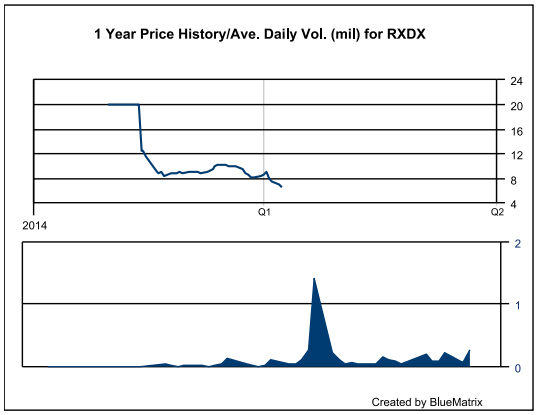
• **While early with limited clinical data, observed ALK activity bodes well for RXDX-101 as a Trk inhibitor.** Preclinical data suggest that RXDX-101 has potent activity (in low nM) against TrkA, TrkB, TrkC, ROS1 and ALK. Initial Phase I clinical data suggested a good safety profile with some activity in ALK+ and ROS1+ solid tumors. Although there are no clinical data against Trk (due to lack of screening capability in the Italian trial), sufficient exposure appears to have been achieved to adequately cover RXDX-101 activity against Trk given that 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.

• **Beyond Trk, ROS1 mutation could represent an interesting opportunity Trk.** ROS1 rearrangement was identified in 1-2% of NSCLC patients, ~9% of cholangiocarcinoma, and other tumors such as ovarian, gastric and colorectal cancers. Although many potent ALK inhibitors also showed activity in ROS1+ tumors, only a handful of compounds are in clinical development. Among these compounds targeting ROS1+, crizotinib showed encouraging data in NSCLC, and KOL feedback was supportive for a potential approval. So far, slightly better activity of RXDX-101 vs. crizotinib has been seen in pre-clinical studies while efficacy against crizotinib resistant patients remains to be seen.

• **Potential to cross BBB could be a differentiating factor.** RXDX-101 showed high brain/blood ratio (0.4-2.2) in several animal models, suggesting potential to cross brain blood barrier (BBB), which may support potent activity in the central nervous system (CNS) in the clinical studies. A high percentage of NSCLC patients develop brain metastasis and activity in the CNS could be a differentiating factor for RXDX-101.

• **Technology platform could generate a sustainable pipeline.** By screening for oncogenic mutations and genetic defects, RXDX is capable of identifying new oncogenic drivers and developing companion diagnostics to advance targeted therapy with integrated Rx/Dx strategy

Key Stats:	**(NASDAQ:RXDX)**
S&P 600 Health Care Index:	**1,244.02**
Price:	**$6.68**
Price Target:	$14.00
Methodology:	Probability-weighted DCF analysis
52 Week High:	$20.00
52 Week Low:	$1.00
Shares Outstanding (mil):	19.6
Market Capitalization (mil):	$130.9
Book Value/Share:	$5.37
Cash Per Share:	$4.96
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	0.0	0.0	0.0	0.0	0.0	($0.33)	($0.36)	($0.43)	($0.47)	($1.61)	NM
2015E	--	--	--	--	0.0	--	--	--	--	($1.92)	NM

Source: Company Information and Leerink Partners LLC Research

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IGNYTA – INITIATION OF COVERAGE WITH OP

APRIL 9, 2014

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RXDX OVERVIEW

- We are initiating coverage on RXDX with an Outperform rating and $14 per share price target.
- RXDX is a biotech company with a focus on targeted therapies and molecular diagnosis in oncology.
- Lead candidate RXDX-101 is a potentially first-in-class oral pan-Trk inhibitor that also has ROS1 and ALK activity.
  - Preclinical data support potent (low nM) inhibition against ROS1, ALK, TrkA, TrkB, and TrkC, as well as penetration into the central nervous system.
  - Initial Phase I data from an Italian study suggest activity in ALK+ and ROS1+ solid tumors.
  - Due to absence of a screening method for Trk rearrangement, no Trk patients were enrolled in the RXDX-101 Phase I trial although in vitro RXDX-101 is approximately 10x more potent against Trk vs. ALK
  - A Phase I/IIa study will be initiated in 3Q:14 with potential to expand to 5 cohorts (ALK naïve, ALK treated, ROS1, TrkA and TrkB/C).
- RXDX-102 as a back-up to RXDX-101 has less CNS penetration and more specific Trk inhibition with less activity against ROS1 and ALK.
- 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.
- Credible management team with significant major pharma & biotech leadership experience, and distinguished academic training.
- Key Financials: 19.6M shares outstanding, ~$97M pro forma cash ($4.96/share).

RXDX INVESTMENT THESIS

- **RXDX's approach of targeting molecular oncogenic drivers has historically resulted in highly effective agents.** Lung cancer treatment is increasingly evolving into targeting molecular drivers. 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 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.
- **Trk is an emerging target for NSCLC and RXDX may have first mover advantage.** We believe the main value for RXDX-101 lies in the market potential for pan-Trk cancers. TrkA rearrangement as a driver oncogene has just emerged following recent discovery (Vaishnavi et al Nat Med 2013, 19:1469). 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 types. RXDX has the potential to develop a first-in-class Trk inhibitor.
- **Although still early with limited clinical data, observed ALK activity bodes well for RXDX-101 as a Trk inhibitor.** Preclinical data suggest that RXDX-101 has potent activity (in low nM) against TrkA, TrkB, TrkC, ROS1 and ALK. Initial Phase I clinical data suggested a good safety profile with some activity in ALK+ and ROS1+ solid tumors. Although there are no clinical data against Trk (due to lack of screening capability in the Italian trial), sufficient exposure appears to have been achieved to adequately cover RXDX-101 activity against Trk given that 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.

RXDX INVESTMENT THESIS

- **Beyond Trk, ROS1 mutation could represent an interesting opportunity Trk.** ROS1 rearrangement was identified in 1-2% of NSCLC patients, ~9% of cholangiocarcinoma, and other tumors such as ovarian, gastric and colorectal cancers. Although many potent ALK inhibitors also showed activity in ROS1+ tumors, only a handful of compounds are in clinical development. Among these compounds targeting ROS1+, crizotinib showed encouraging data in NSCLC and our KOL feedback was supportive for a potential approval. So far, slightly better activity of RXDX-101 vs. crizotinib has been seen in pre-clinical studies while efficacy against crizotinib resistant patients remains to be seen.

- **Numerous potent 2nd generation ALK inhibitors set high bar for RXDX-101 clinical development in crizotinib resistant NSCLC.** Currently, there are at least 9 second generation ALK inhibitors in clinical development, where NVS's (OP) ceritinib (LDK378) was recently filed for approval, and Chugai/Roche's CH5424802 and ARIA's (MP) AP26113 are in Phase II development. Response rates from these agents are in the range of 58-75% in crizotinib pretreated ALK+ NSCLC patients and 60-94% in crizotinib native ALK+ patients. Additionally, all three compounds showed various degree of activity in the central nervous system.

- **Potential to cross BBB could be a differentiating factor.** In animal studies, RXDX-101 showed potential to cross brain blood barrier (BBB) with brain/blood ratio reaching 0.4-2.2 in mouse, rat and dog, which may support potent activity in the CNS in clinical studies. Since a high percentage of NSCLC patients develop brain metastasis, activity in the CNS could be an important differentiating factor for RXDX-101.

- **Technology platform could generate a sustainable pipeline.** By screening for oncogenic mutations and genetic defects, RXDX is capable of identifying new oncogenic drivers and developing companion diagnostics to further advance targeted therapy with integrated Rx/Dx strategy.

RXDX 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 $97M cash 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.

RISKS 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 – RXDX has pro forma cash of $97M as of 1Q:14, sufficient to fund operations into 2016 before commercialization which will require additional capital.

PIPELINE FOCUSING ON TARGETED THERAPY

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 dosing in 6-24 pts with Trk, ROS, or ALK alterations to be initiated in 3Q: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
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

KEY EXPECTED EVENTS – DATA NEWS FLOW

Timing	Event
RXDX-101 (Pan-Trk, ROS1, ALK inhibitor)	
3Q:14	Initiation of STARTRK-1 Phase I/II dose escalation study with continuous dosing
4Q:14	Phase I update from the Italian trial
	Basket Trial expansion cohorts in TrkA, TrkB, TrkC, ROS1, ALK
ASCO 2015	STARTRK data
Spark-1 (Rx/Dx novel target)	
2015	IND candidate

Source: Company Reports

INVESTMENT CONSIDERATION #1

NSCLC TREATMENT PARADIGM IS EVOLVING

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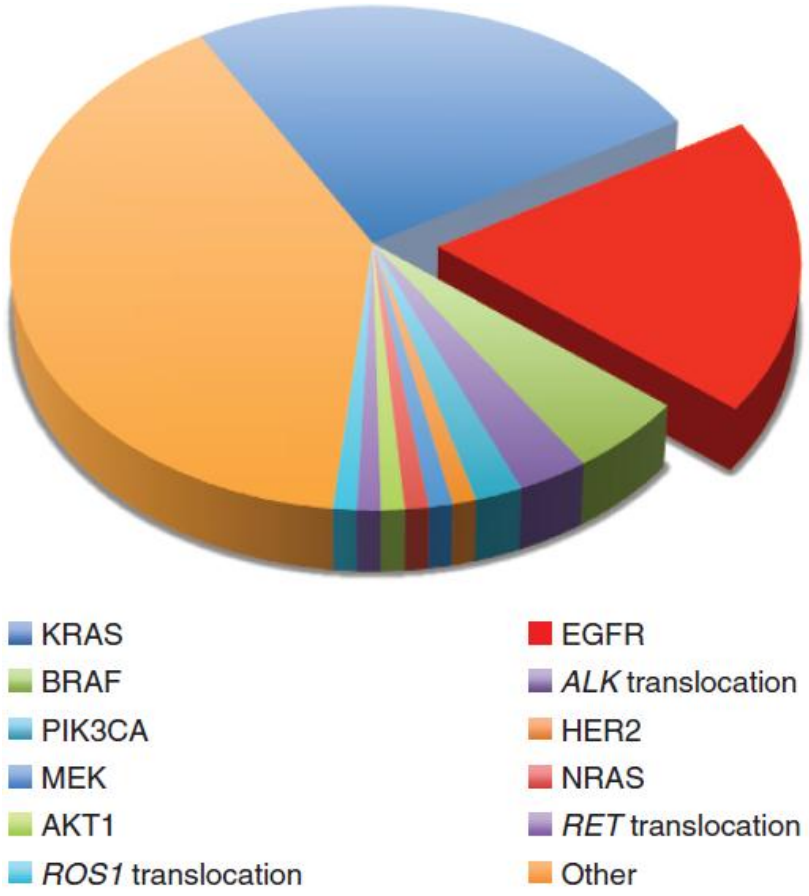
ONCOGENE DRIVERS HAVE BEEN IDENTIFIED IN ~70% LUNG ADENOCARCINOMA

Gene	Alteration	Frequency in NSCLC
AKT1	Mutation	1%
ALK	Rearrangement	3–7%
BRAF	Mutation	1–3%
DDR2	Mutation	~4%
EGFR	Mutation	10–35%
FGFR1	Amplification	20%
HER2	Mutation	2–4%
KRAS	Mutation	15–25%
MEK1	Mutation	1%
MET[a]	Amplification	2–4%
NRAS	Mutation	1%
PIK3CA	Mutation	1–3%
PTEN	Mutation	4–8%
RET	Rearrangement	1%
ROS1[a]	Rearrangement	1%



Drugs approved in NSCLC.
Drugs approved in NSCLC but for other molecular subtype.
Drugs approved in other cancer.
Drugs in clinical development.

Source: http://www.mycancergenome.org/content/disease/lung-cancer; Blakely et al, Cancer Discovery (2012) 2:872-875

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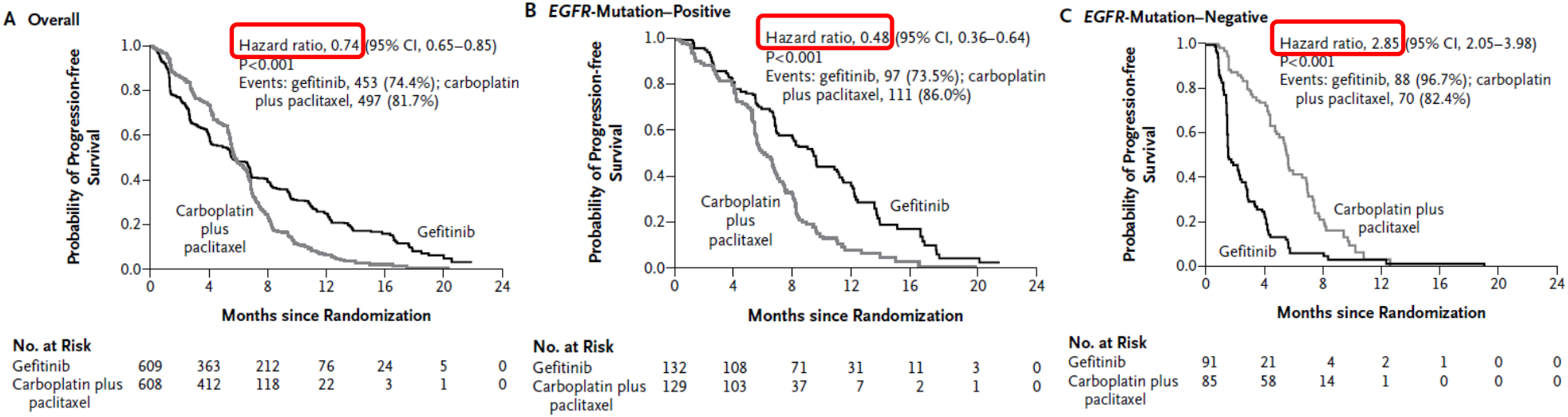
IN UNSELECTED FIRST-LINE NSCLC, 4 LARGE STUDIES OF EGFR TKIS SHOWED NO SIGNS OF EFFICACY WHEN ADDED TO CHEMOTHERAPY

	TRIBUTE[1]		TALENT[2]		INTACT-1[3]			INTACT-2 [4]		
Chemotherapy doublet	**Carboplatin/paclitaxel**		**gemcitabine/cisplatin**		**gemcitabine/cisplatin**			**Carboplatin/Paclitaxel**		
	Placebo	**Tarceva**	**Placebo**	**Tarceva**	***placebo***	***Iressa[2] 500mg/d***	***Iressa 250 mg/d***	***placebo***	***Iressa[3] 500mg/d***	***Iressa 250 mg/g***
Patients	*533*	*526*	*579*	*580*	324	330	336	345	347	345
Median survival	10.6	10.5	11.0	10.8	10.9	9.9	9.9	9.9	8.7	9.8
		HR=0.995		HR=1.06						
p-value		*p=0.95*		*p=0.49*		*p=0.456*			*p=0.64*	
Med TTP	4.8	5.1	6.2	5.9	6	5.5	5.8	5.0	4.6	5.3
		HR=0.937		HR=0.98						
p-value		*p=0.36*		*p=0.74*		*p=0.763*			*p=0.0562*	
One-year survival	44%	47%	42%	41%	44%	43%	41%	42%	37%	41%
ORR (PR+CR)	19.3%	21.5%	29.9%	31.5%	47.2%	50.3%	51.2%	28.7%	30.0%	30.4%
Duration of treatment- weeks	18	21	--	--	22.7	13.6	21.4	19.7	14.1	18.4

Source: 1. Herbst et al. JCO 2005;2. Gatzemeier U et al. JCO 2007; 3. Giaccone et al. JCO 2004; 4. Herbst et al. JCO 2004

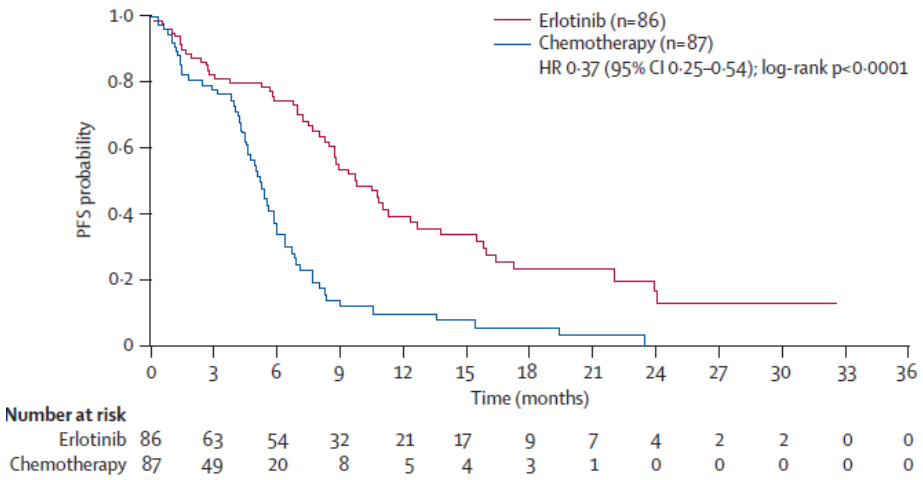
IPASS DATA PROVIDE A STRIKING EXAMPLE OF THE BENEFIT OF SELECTING TREATMENT BASED ON MOLECULAR DRIVER

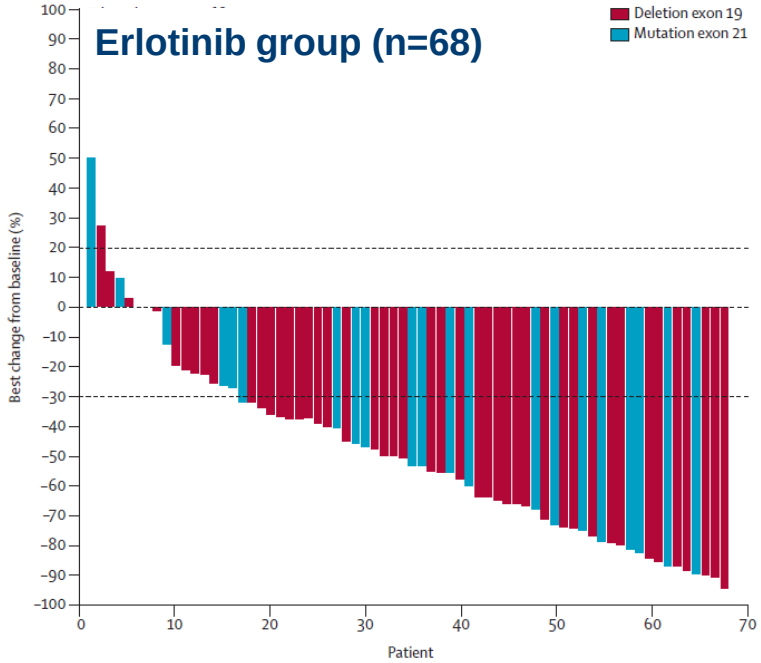
- In a randomized large scale (1,217) Phase III IPASS trial comparing gefitinib (Iressa) vs. carboplatin/ paclitaxel as a first line treatment in East Asian NSCLC patients, overall PFS results favored gefitinib and this benefit seems to be driven by EGFR activating mutation (~60% of patients).

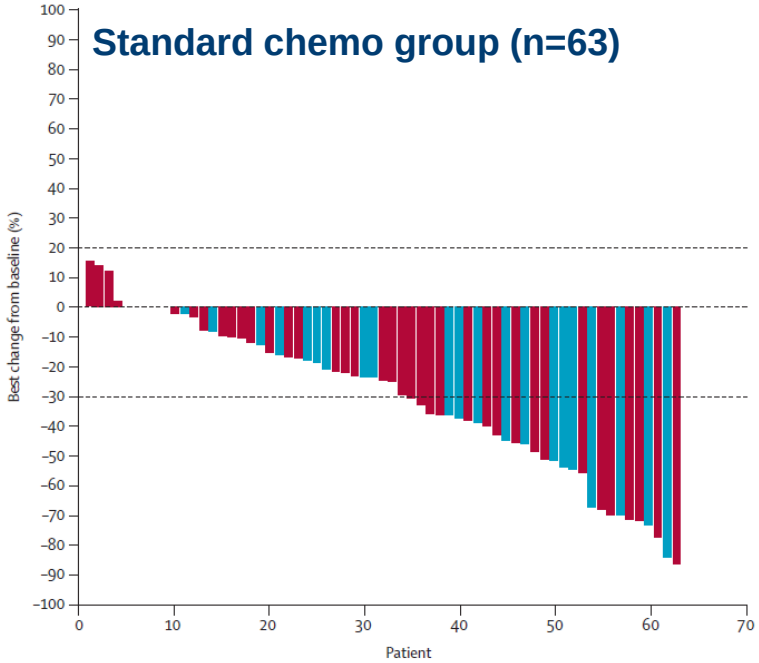


Source: Mok et al, NEJM (2009) 361:947

TARCEVA WAS SUPERIOR TO CHEMO BY A LARGE MARGIN IN A STUDY OF EUROPEAN NSCLC PATIENTS WITH EGFR MUTATION



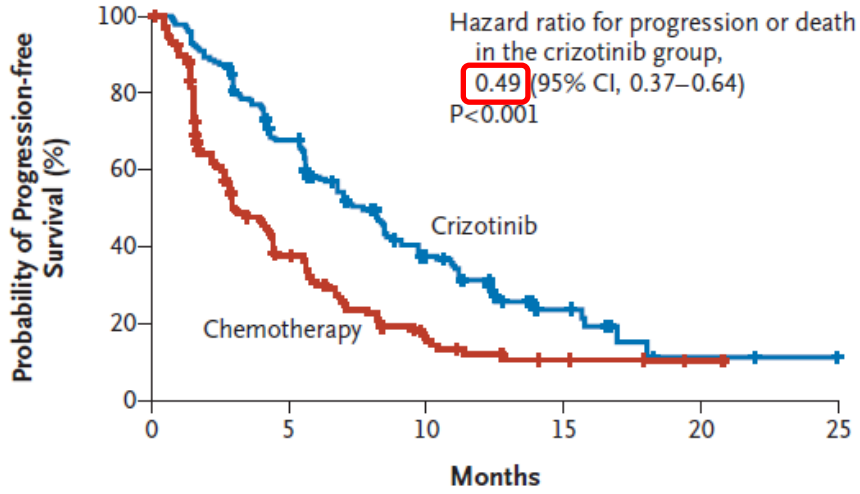




Source: Rosell et al, Lancet Oncology (2012) 13:239

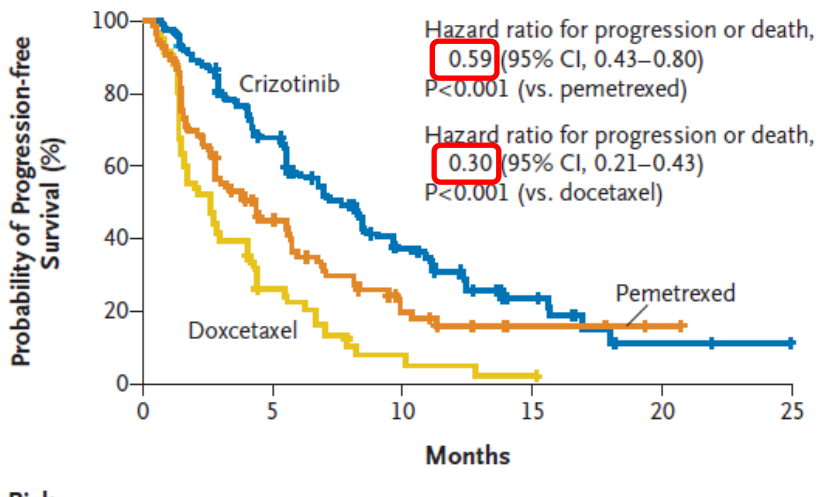
XALKORI DATA PROVIDE ANOTHER EXAMPLE WHERE A TARGETED AGENT SHOWED SUPERIOR EFFICACY TO CHEMO IN SELECTED PATIENTS (ALK)

A Progression-free Survival



No. at Risk						
Crizotinib	173	93	38	11	2	0
Chemotherapy	174	49	15	4	1	0

B Progression-free Survival with Crizotinib vs. Pemetrexed or Docetaxel



No. at Risk						
Crizotinib	172	93	38	11	2	0
Pemetrexed	99	36	2	3	1	0
Docetaxel	72	13	3	1	0	

Source: Shaw et al, NEJM (2013) 368:2385

VALIDATED APPROACH SUPPORTED BY PRECEDENT OF SUCCESSFUL CASES IN TARGETED THERAPIES IN NSCLC

- Currently, three drugs have been approved by the FDA as targeted therapies in NSCLC patients with select biomarkers.
- All three drugs showed significant improvement of overall response rate (ORR) and progression-free survival (PFS) vs. chemotherapy.
- ORR among all studies exceeded 50% while the control groups were below 20%.
- Following accelerated approval for Xalkori (2011) in ALK+ front line NSCLC based on two single-arm studies, the FDA approved new indication for Tarceva for first-line treatment of NSCLC harboring EGFR mutations. Shortly after, the FDA also approved Gilotrif (under priority review) for the treatment of NSCLC with EGFR mutations based on data from a control study.
- Historical evidence suggests that targeted therapies in NSCLC could provide better-than-average chances for success.

Target	Approved Drug	ORR Drug/Chemo	PFS (mon) Drug/Chemo	Approval on Select Biomarker
EGFR	Tarceva (erlotinib)	65% / 16%	10.4 / 5.2	May, 2013 (initial approval Nov, 2004)
	Gilotrif (afatinib)	50% / 19%	11.1 / 6.9	July, 2013
ALK	Xalkori (crizotinib)	65% / 20%	7.7 / 3.0	Aug, 2011

Source: Drug labels, Leerink Partners

INVESTMENT CONSIDERATION #2

TRK IS AN EMERGING TARGET

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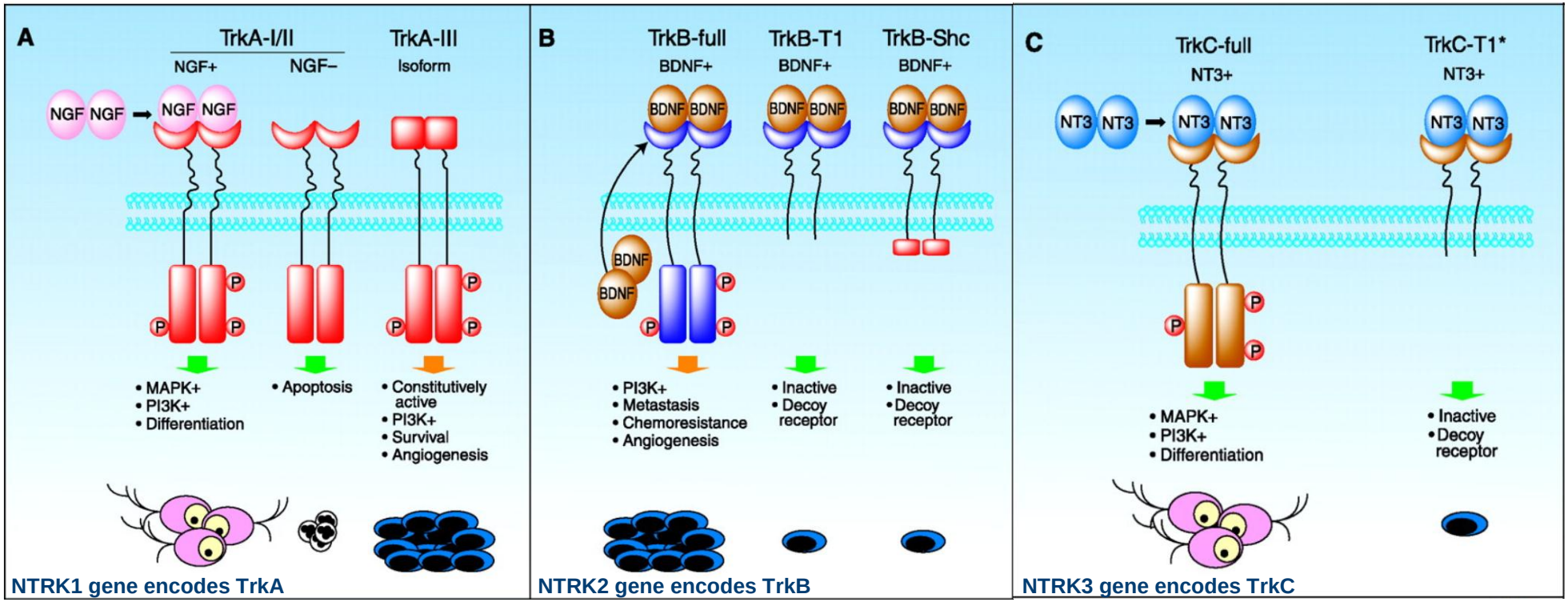
TRK IS A NEWLY DISCOVERED TARGET WITH STRONG EVIDENCE AS AN ONCOGENIC DRIVER

- TrkA as a driver oncogene was unclear until recent breakthrough discovery in NSCLC by Dana-Farber Cancer Institute and University of Colorado Cancer Center (Vaishnavi et al Nat Med 2013, 19:1469). In an elegantly designed study, TrkA rearrangement caused tumorogenesis in a xenograft mouse model and turning off the active domain of rearranged TrkA resulted in an absence of tumor development, suggesting that TrkA is the oncogenic driver for TrkA rearrangement. This conclusion is further supported by the identification of TrkA rearrangement in NSCLC patients who lack any known oncogenic mutations.
- TrkA rearrangement has only recently emerged as a target and some cancer centers have started to screen TrkA rearrangement in NSCLC as well as in other cancers. In addition to TrkA, FISH (fluorescent in situ hybridization) screening technology for TrkB and TrkC rearrangement is also in development.
- Initial assessment suggests that incidence of TrkA rearrangement likely occurs in 1% of NSCLC, although feedback from some KOLs is mixed (some believe the rate is lower while others think it could be higher). Various studies as well as internal data from RXDX suggest that TrkA rearrangement occurs in 2-3% of colorectal cancer adenocarcinoma, and 12% of papillary thyroid cancer. Cases of TrkB and TrkC rearrangement have also been identified; however, incidence rates are unclear.
- In addition to Trk rearrangement, overexpression of TrkB has been studied in many cancer indications including triple negative breast cancer. In aggregate, Trk rearrangement and overexpression represent a $1-2B market opportunity.
- Although many compounds have activity against Trk, so far only a handful of companies are dedicated to developing Trk targeted therapies.

TrkA, TrkB, TrkC ISOFORM EXPRESSION AND ACTIVATION



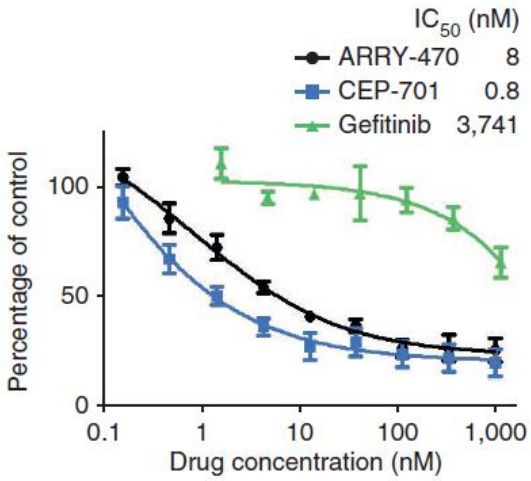
- A – Activation of TrkA-I (neuronal) or TrkA-II (non-neuronal) receptor isoforms by ligand NGF (nerve growth factor) leads to TrkA activation and signaling, ultimately resulting in survival and neuronal differentiation. In the absence of ligand, alternative pathways are activated and leading to apoptosis. The TrkA-III isoform is constitutively active, ligand independent, and promotes survival mainly through the PI3K-AKT pathway.
- B – Two full-length TrkB isoforms are activated in neuroblastomas by BDNF (brain derived neurotrophic factor). The truncated, kinase-deficient TrkB isoforms (TrkB-T1 and TrkB-SHC) contain the ligand binding site, and may inhibit activation either by competing for ligand binding or by forming functionally inactive heterodimers with full-length TrkB.
- C – Two major kinase-active TrkC isoforms are activated by signaling from NT3 (neurotrophin-3), promoting survival and differentiation. Truncated isoforms (predominantly TrkC-T1) function as inactive decoy receptors by mechanisms similar to the truncated TrkB receptors.

Source: Brodeur et al, Clin Cancer Res (2009) 15:3244

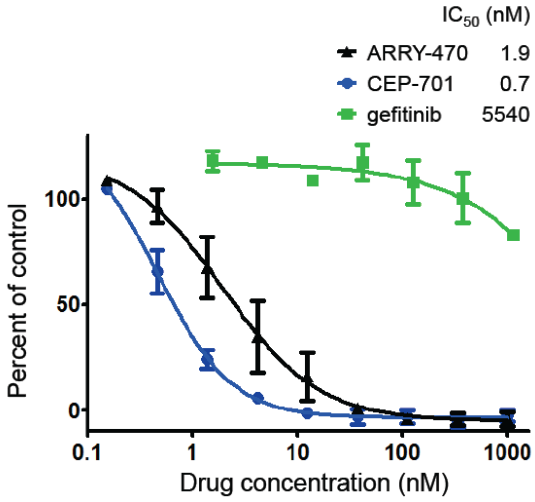
TrkA REARRANGEMENT IS IDENTIFIED AS NEW ONCOGENIC DRIVER IN LUNG CANCER

- In 91 lung cancer patients without known oncogenic alterations, three (3.3%, or ~1% in overall lung cancer patients) tumor samples showed evidence of NTRK1 gene fusions.
- MPRIP-NTRK1 and CD74-NTRK1 fusions lead to constitutive TrkA activation. Treatment of cells expressing NTRK1 fusions with TrkA inhibitor inhibited autophosphorylation of TrkA and cell growth.
- Cell culture studies (Ba/F3 cells expressing the MPRIP-NTRK1 fusion and CD71-NTRK1 fusion, KM12 cells expressing TPM3-NTRK1 fusion) demonstrate inhibition of proliferation by pan-Trk inhibitor ARRY-470 and CEP-701 with IC_{50} in nM range, while gefinib (EGFR inhibitor) showed no inhibition.

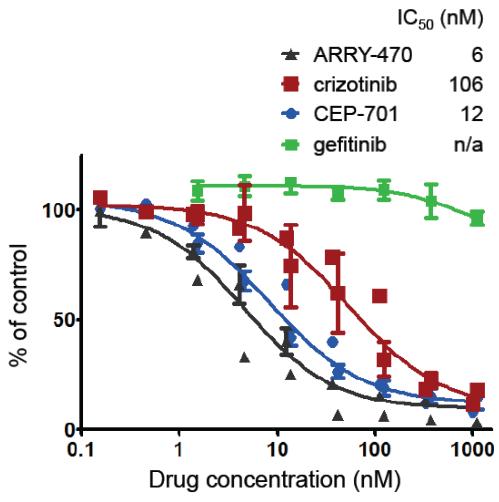
Ba/F3 cells (RIP-TRKA fusion) (NSCLC)



Ba/F3 cells (CD74-TRKA fusion) (NSCLC)



KM12 cells (TPM3-TRKA fusion) (Papillary thyroid cancer)



Source: Vaishnavi et al, Nat Med (2013) 19:1469

TRKA REARRANGEMENT IS IDENTIFIED AS NEW ONCOGENIC DRIVER IN LUNG CANCER

- TrkA rearrangement such as MPRIP-NTRK1 or CD74-NTRK1 gene fusions (see below RIP-TRKA and CD74-TRKA) induce tumor growth in nude mouse model.
- When turning of the activity domain of TrkA (Kinase Dead domain), TrkA rearrangement (RIP-TRKA) can no longer generate tumors (see below RIP-TRKA-KD), suggesting TrkA is the oncogenic driver.

Source: Vaishnavi et al, Nat Med (2013) 19:1469

TRK REARRANGEMENT HAS BEEN IDENTIFIED IN EPITHELIAL CANCERS

TRK REARRANGEMENT IN EPITHELIAL CANCERS

Kinase (location)	Malignancy	Rearrangement partners	Location of partners	Type of rearrangement	Frequency*	Refs
NTRK1 (1q21-22)	Colorectal cancer	*TPM3*	1q21.2	Paracentric inversion	-	160
	Papillary thyroid cancer	*TPM3*	1q21.2	Paracentric inversion	12%	40,161, 162,163
		TPR	1q25	Paracentric inversion		
		TFG	3q12.2	Interchromosomal		
	Lung adenocarcinoma	*MPRIP*	17p11.2	Interchromosomal	-	135
		CD74	5q32	Interchromosomal	-	
NTRK3 (15q25)	Secretory breast cancer	*ETV6*	12p13	Interchromosomal	-	2
	Salivary gland tumour	*ETV6*	12p13	Interchromosomal	-	164

Source: Shaw et al, Nat Rev Cancer (2013) 13:772

MARKET POTENTIAL FOR TRKA REARRANGMENT AND TRKB OVER EXPRESSION

TrkA Rearrangement	US Incidence	% of TrkA Rearrangement	Incidence of TrkA Rearrangement	Cost per Course	Market Potential ($M) - TrkA
NSCLC	193,962	1%	2,240	101,200	227
Recurrence/Metastases Papillary thryoid cancer	10,833	12%	1,300	126,500	164
CRC adenocarcinoma	123,147	2%	2,463	101,200	249
Market Potential ($M)			**6,003**		**640**
TrkB Overexpression	**US Incidence**	**% of TrkB Overexpression**	**Incidence of TrkB Overexpression**	**Cost per Course**	**Market Potential ($M) - TrkB**
TNBC	11,692	84%	9,821	101,200	994
Market Potential ($M)			**9,821**		**994**
Total Market Size ($M)					**1,634**

Source: Company Reports, ClinicalTrial.gov, Leerink Partners

LEERINK

NUMEROUS TRK INHIBITORS BUT LIMITED DEVELOPMENT FOCUSING ON TRK

Trk Inhibitors	Company	IC_{50} - Kinase Assay (nM)					IC_{50} - KM12 (TPM3-TRKA) (nM)	IC_{50} - Ba/F3 (CD74-TRKA) (nM)	IC_{50} - Ba/F3 (RIP-TRKA) (nM)	Stage of Development	NCT
		TrkA	TrkB	TrkC	ROS1	ALK					
Crizotinib	PFE						106			No Trk-specific cohorts or trials ongoing	NA
ARRY-470	ARRY						6	1.9	8	NA	NA
AZ-23	AZN									halted due to poor PK properties	NA
Dovitinib	NVS									Phase II in solid tumors including FGFR, PDGFR, VEGF, cKIT, FLT3, CSFR1, Trk and RET	NCT01831726
Lestaurtinib (CEP-701)	Cephalon						12	0.7	0.8	No Trk-specific cohorts or trials ongoing	NA
Loxo-101	Loxo Oncology									Phase I/II in TrkA, TrkB or TrkC	NA
PLX7486	Plexxikon/ Daiichi Sankyo									Phase I/II in Fms and TrkA, TrkB and TrkC in combo with gemcitabine and Abraxane in solid tumors (pancreatic cancer expansion cohort)	NCT01804530
TSR-011	TSRO	0.5	1.5	2.4		0.4	25	1.8		Phase I/IIa in 1) ALK-positive, ALKi naïve NSCLC, 2) ALK+ NSCLC who progressed on another ALKi, 3) Solid tumors or lymphomas with either ALK+ or Trk mutations	NCT02048488
RXDX-101	RXDX	1	2	5	7	12	22			Phase I/IIa in 1) TrkA, 2) TrkB/C, 3) ROS1, 4) ALK+, ALKi naïve, 5) ALK+, ALKi treated	NCT02097810
RXDX-102	RXDX									Preclinical	NA
GTx-186	GTXI	1.1	2.1	1.6	0.2	4.5				Preclinical	NA

Source: Company Reports, ClinicalTrial.gov, Leerink Partners

INVESTMENT CONSIDERATION #3

BREADTH AND STRENGTH OF RXDX-101 PHASE I DATA

RXDX-101 – INITIAL CLINICAL EVIDENCE OF ACTIVITY AGAINST ALK AND ROS1 IN CRIZOTINIB NAÏVE PATIENTS

Dose Cohort (mg/m^2)	# of Treated Patients	Molecular Alteration	Tumor Types	Prior ALK inhibitors	Status / Notable Preliminary Observations
100	3	ALK or ROS1 rearrangements	NSCLC; Other	2 on Crizotinib; None	• All discontinued for PD
200	3	ALK mutation; ALK rearrangement; ROS1 amplification	NSCLC; Other	None	• Neuroblastoma (ALK+) patient in Cycle 14 with PR; increased to 400mg/m^2 (Cycle 6), 800 mg/m^2 (Cycle 12), 1200 mg/m^2 (Cycle 14) • NSCLC (ALK+) patient in Cycle 12 with prolonged SD; increased to 400 mg/m^2 (Cycle 5) and 800 mg/m^2 (Cycle 12)
400	4	ALK or ROS1 deletions	NSCLC; Other	None	• Pancreatic cancer ($ROS1^{del}$) patient in Cycle 9 with prolonged SD
800	3	ALK rearrangements or mutation	NSCLC; Other	Crizotinib & LDK; Crizotinib; None	• All discontinued for PD
1200	3	ALK or ROS1 rearrangements	NSCLC	Crizotinib & LDK; Crizotinib; None	• All 3 active in Cycles 2 – 3 • 1 patient de-escalated to 800 mg/m^2 due to Grade 3 AE (asthenia) in Cycle 2
1600	1	ALK rearrangement	NSCLC	Crizotinib	• Active in Cycle 1

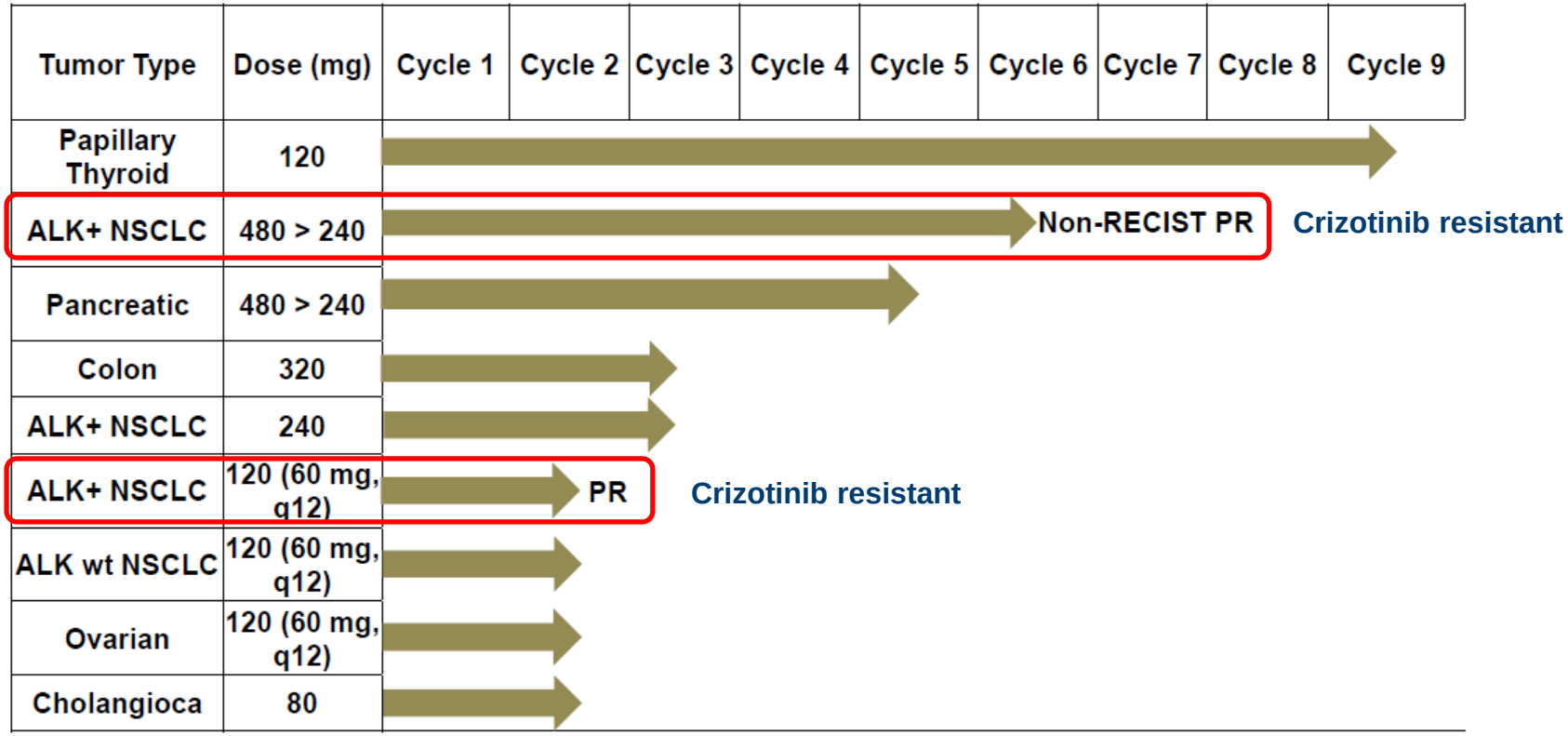
Dosing: 4-week cycle with oral daily 4 days on, 3 days off for 3 weeks, then 1 week rest

Source: Company Reports, Gainor et al, IASLC 2014,; Note: data as of Feb 18, 2014

RXDX-101 – KEY TAKEAWAYS FROM THE PHASE I DATA

- Good safety profile with truncated dosing regimen
  - Dosing 4-week cycle with oral daily 4 days on, 3 days off for 3 weeks, then 1 week rest
  - Truncated dosing was designed based on toxicity (mainly CNS) observed in preclinical studies
  - Despite dose reaching 1,600mg/m^2, only one patient had Grade 3 asthenia
  - No dose limiting toxicity has been reached yet
  - Our MEDACorp KOL considered lack of neurotoxicity as the most important key takeaway given that NTRK2 is expressed in the brain and RXDX-101 appears to be able to cross BBB
- Initial activity seen in crizotinib naïve ALK+ and ROS1+ patients
  - One partial response in neuroblastoma (ALK+)
  - One stable disease in NSCLC (ALK+)
  - One stable disease pancreatic cancer (ROS1+)
  - Activity in crizotinib resistant patients has yet to be seen
- Although no data on patients with Trk rearrangement (due to lack of screening capability), given that activity against ALK has already been shown and RXDX-101 in vitro activity (IC50) is 10x more potent against Trk, it suggests that current dosing has sufficient exposure to adequately cover Trk.

TSR-011 (TSRO) PHASE I DATA SHOWED ACTIVITY AGAINST CRIZOTINIB RESISTANT NSCLC PATIENTS



Source: Weiss et al, ESMO 2013

TSR-011 (TSRO) PHASE I SAFETY DATA INDICATED DLT RELATED TO QTC PROLONGATION

Summary of Dose Limiting Toxicities (DLT*) And Grade ≥2 Related Adverse Events

	Dose (in mg; schedule is once daily unless otherwise indicated)							
Adverse Event	30 (n=1)	60 (n=1)	80 (n=3)	120 (n=1)	60 q12hr (n=3)	240 (n=4)	320 (n=3)	480 (n=4)
Anorexia	-	-	-	-	-	n=1	-	-
Peripheral Neuropathy	-	-	-	-	-	n=1	-	-
Dysaesthesia	-	-	-	-	-	n=1 (DLT)	-	-
Fatigue/Asthenia	-	-	-	n=1	-	n=1	-	-
QTc prolongation	-	-	-	-	-	n=1	n=1 (DLT)	n=2 (DLT)

**DLT is defined (per protocol) as occurring in Cycle 1, drug-related and Grade ≥3*

Source: Weiss et al, ESMO 2013

DATA COMPARISON – RXDX-101 VS. TSR-011

- Comparable preclinical activity against Trk
  - Enzymatic assay data indicate similar IC_{50} (single digit nM range) against TrkA/B/C
  - IC_{50} data in KM12 cells (~22-25nM) suggest similar activity against TrkA rearrangement
- TSR-011 appears to have better potency against ALK
  - Enzymatic IC_{50} of 0.4nM vs. 12nM for RXDX-101
  - PR in crizotinib-resistant ALK+ pts while RXDX-101 activity only seen in crizotinib naïve pts
- RXDX-101 safety profile (truncated dosing) appears better than TSR-011
  - Reached 1,600mg/m^2 with no DLT while TSR-011 reached maximum tolerated dose (MTD) with QTc prolongation as DLT
- Trk clinical activity is unknown for both drugs

Trk Inhibitors	Company	IC_{50} - Kinase Assay (nM)					IC_{50} - KM12 (TPM3-TRKA) (nM)	IC_{50} - Ba/F3 (CD74-TRKA) (nM)	Stage of Development	NCT
		TrkA	TrkB	TrkC	ROS1	ALK				
TSR-011	TSRO	0.5	1.5	2.4		0.4	25	1.8	Phase I/IIa in 1) ALK-positive, ALKi naïve NSCLC, 2) ALK+ NSCLC who progressed on another ALKi, 3) Solid tumors or lymphomas with either ALK+ or Trk mutations	NCT02048488
RXDX-101	RXDX	1	2	5	7	12	22		Phase I/IIa in 1) TrkA, 2) TrkB/C, 3) ROS1, 4) ALK+, ALKi naïve, 5) ALK+, ALKi treated	NCT02097810

Source: Weiss et al, ESMO 2013, Gainor et al, IASLC 2014

RXDX-101 PHASE I/IIa STARTRK-1 AND STARTRK-2 TRIAL DESIGN

ALKA-372-001

Phase 1 dose escalation study of intermittent dosing schedule in Italy: 20-30 cancer patients with ALK, ROS1 or TrkA alterations

STARTRK-1 NCT02097810

Global Phase 1/2 study in U.S., EU and Asia

- Dose escalation of daily continuous dosing schedule in 6-24 patients with Trk, ROS1 or ALK molecular alterations
- "Basket trial" expansion cohorts in 100 patients with TrkA, TrkB, TrkC, ROS1 or ALK molecular alterations, treated with RP2D*

(To be initiated in 3Q:14)

STARTRK-2 and Beyond

- Pivotal registration studies in most promising tumor types and targets based on ORR* and other clinical observations
- Accelerated approval and/or breakthrough therapy designation possible

Note: RP2D – recommended Phase II dose; ORR – objective response rate
Source: Company Reports and ClinicalTrial.gov

KEY CONSIDERATIONS FOR RXDX-101 STARTRK-1 STUDY

- Continuous dosing should shift therapeutic window in lower dose range
  - In truncated dosing regimen (100-1,600mg/m^2), therapeutic window falls in higher doses tested in the Italian trial
  - With new continuous dosing regimen, therapeutic window should shift to lower doses, likely below 1,000mg/m^2
  - Although the starting dose has not been disclosed, management indicated that initial dose should be in low single-digit hundreds
  - We may start to see activity in lower dose, and potentially activity against crizotinib-resistant pts
- Continuous dosing may introduce new toxicity
  - Although RXDX-101 appears very safe with truncated dosing, initial concerns (CNS toxicity) that led to the truncated design may re-emerge, given that Trk proteins are expressed in the brain and RXDX-101 appears to be able to cross BBB based on preclinical data.
- TrkA/B/C rearrangement (vs. over-expression) will likely be the initial target
  - Our MEDACorp KOLs considered TrkA/B/C rearrangement as a better validated oncogenic driver
  - Management indicated enrolling tumor types with likely Trk molecular alteration, which leads to NSCLC, papillary thyroid cancer and colorectal cancer (CRC) as top candidates

INVESTMENT CONSIDERATION #4

CRIZOTINIB PROVIDES PRECEDENT FOR ROS1 AS A TARGET

ROS1 REARRANGEMENT OCCURS IN MULTIPLE EPITHELIAL CANCERS

ROS1 (6q22)	NSCLC	*SLC34A2*	4p15.2	Interchromosomal	1–2%	4,8, 68, 128,146, 147
		CD74	5q32	Interchromosomal		
		TPM3	1q21.2	Interchromosomal		
		SDC4	20q12	Interchromosomal		
		EZR	6q25.3	Paracentric inversion		
		LRIG3	12q14.1	Interchromosomal		
		FIG	6q21	Deletion		
		KDELR2	7p22.1	Interchromosomal		
		CCDC6	10q21	Interchromosomal		
	Cholangiocarcinoma	*FIG*	6q21	Deletion	8.7%	129
	Ovarian cancer	*FIG*	6q21	Deletion	-	148
	Gastric cancer	*SLC34A2*	4p15.2	Interchromosomal	-	149
	Colorectal cancer	*SLC34A2*	4p15.2	Interchromosomal	-	140

Source: Shaw et al, Nat Rev Cancer (2013) 13:772

MARKET POTENTIAL FOR ROS1 REARRANGMENT

ROS1 Rearrangement	US Incidence	% of ROS1 Rearrangement	Incidence of ROS1 Rearrangement	Cost per Course	Market Potential ($M) - ROS1
NSCLC	193,962	1.5%	2,909	101,200	294
Cholangiocarcinoma	3,000	8.7%	261	101,200	26
Market Potential			**3,170**		**321**

Source: Company Reports, ClinicalTrial.gov, Leerink Partners

ALK INHIBITORS GENERALLY HAVE ANTI-ROS1 ACTIVITY

ALK AND/OR ROS1 TYROSINE KINASE INHIBITORS IN THE CLINIC

Drug	Company	ROS1 activity?	Status	Ongoing studies	NCT identifier*	Refs
Crizotinib	Pfizer	Yes	Approved for ALK-positive NSCLC; investigational for ROS1	Phase I for ROS1 and MET	00585195	86, 105
				Phase III for ALK-positive NSCLC comparing crizotinib with first-line chemotherapy	01154140	
LDK378	Novartis	Yes	Investigational (breakthrough therapy designation)	Phase I for ALK	01283516	100, 165
				Phase II for ALK-positive NSCLC, crizotinib-naive	01685138	
				Phase II for ALK-positive NSCLC, crizotinib-treated	01685060	
				Phase III for ALK-positive NSCLC comparing LDK378 with chemotherapy, crizotinib-naive	01828099	
				Phase III for ALK-positive NSCLC comparing LDK378 with chemotherapy, crizotinib-treated	01828112	
CH5424802	Chugai	No	Investigational	Phase I and Phase II study for ALK	01588028	97
AP26113	Ariad	Yes	Investigational	Phase I and Phase II for ALK, ROS1 and other solid tumours	01449461	99
ASP3026	Astellas	Yes	Investigational	Phase I for ALK, ROS1 and other solid tumours	01284192	166
X-396	Xcovery	Yes	Investigational	Phase I for ALK and other solid tumours	01625234	167
TSR-011	Tesaro	Unknown	Investigational	Phase I and Phase II for ALK		168

ALK, anaplastic lymphoma kinase; NSCLC, non-small-cell lung cancer. *See the ClinicalTrials.gov website.

Source: Shaw et al, Nat Rev Cancer (2013) 13:772

CRIZOTINIB ACHIEVED ORR OF 60% IN NSCLC PATIENTS WITH ROS1 REARRANGEMENT, SIMILAR TO DATA IN ALK+ PATIENTS

Table 2. Best overall response to crizotinib.

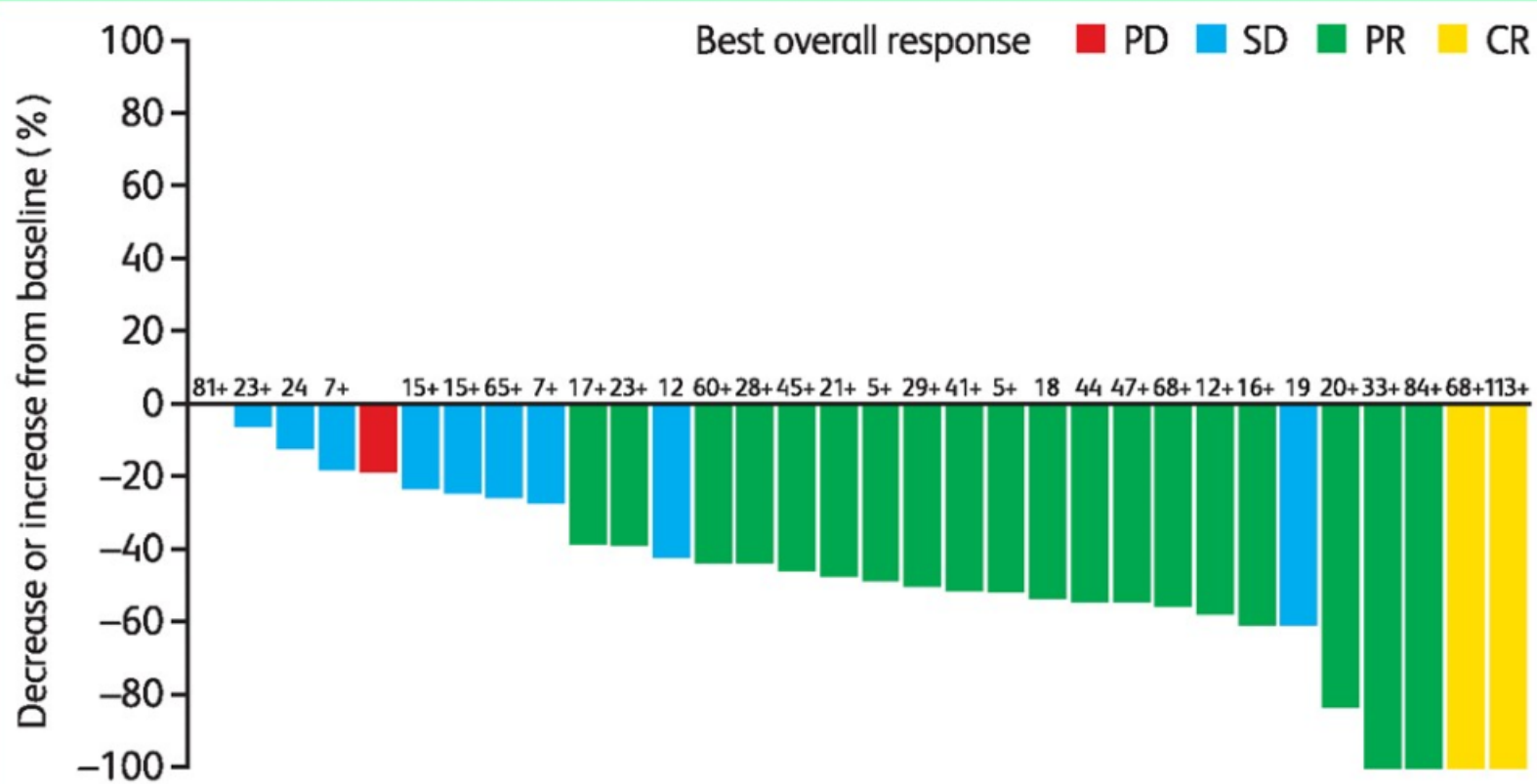
Best response (RECIST v1.0)	Number of patients (n=35)
CR	2 (6)
PR	19 (54)
SD	10 (29)
PD	1 (3)
Indeterminate response	2 (6)
Early death	1 (3)
ORR, % (95% exact CI)	60 (42–76)

ORR (CR + PR).

Source: Ou et al, 2013 ASCO, #8032

CRIZOTINIB WATERFALL PLOT SHOWS DURABLE RESPONSE

Figure 2. Waterfall plot showing tumor responses and duration of response (response-evaluable patients; n=32[a]).



Duration of response (CR and PR) and duration of SD shown in weeks; +, treatment ongoing: for ongoing patients, duration of response/SD is the time from first documentation of tumor response/first dose to last available on-treatment scan; for discontinued patients, duration is to the time of PD or death.
[a]Excludes one patient with early death and two patients with indeterminate response from the response-evaluable group.

Source: Ou et al, 2013 ASCO, #8032

CRIZOTINIB SAFETY PROFILE IN LINE WITH DATA IN ALK+ NSCLC

Table 3. Treatment-related AEs in ≥10 % of patients by MedRA preferred term.

Event	Grade 1, n (%)	Grade 2, n (%)	Grade 3, n (%)	Total, n (%)
Visual impairment	32 (80)	0	0	32 (80)
Diarrhea	14 (35)	0	0	14 (35)
Nausea	10 (25)	2 (5)	0	12 (30)
Peripheral edema	9 (23)	2 (5)	0	11 (28)
Constipation	8 (20)	1 (3)	0	9 (23)
Vomiting	7 (18)	1 (3)	1 (3)	9 (23)
AST increased	5 (13)	1 (3)	1 (3)	7 (18)
Dizziness	7 (18)	0	0	7 (18)
ALT increased	2 (5)	2 (5)	2 (5)	6 (15)
Dysgeusia	6 (15)	0	0	6 (15)
Hypophosphatemia	0	2 (5)	4 (10)	6 (15)
Fatigue	4 (10)	1 (3)	0	5 (13)
Blurred vision	3 (8)	1 (3)	0	4 (10)

There were no treatment-related grade 4 or grade 5 AEs.
ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Source: Ou et al, 2013 ASCO, #8032

OTHER COMPOUNDS SHOWED POTENT ACTIVITY AGAINST ROS1

	HCC78 SLC34A2-ROS1	Ba/F3 FIG-ROS1	Ba/F3 CD74-ROS1	Ba/F3 SDC4-ROS1	Ba/F3 EZR-ROS1
	GI_{50} (nM)	IC_{50} (nM)	IC_{50} (nM)	IC_{50} (nM)	IC_{50} (nM)
AP26113	95 ± 14	31 ± 15	18 ± 3	16 ± 2	41 ± 1
Crizotinib	132 ± 36	45 ± 21	25 ± 12	17 ± 1	52 ± 4
ASP3026	847 ± 126	137 ± 31	55 ± 9	87 ± 10	185 ± 25
CH5424802	1758 ± 518	1021 ± 1056	1864 ± 992	757 ± 211	>10000

	FIG-ROS1 (IC_{50}, nM)		CD74-ROS1 (IC_{50}, nM)	
	WT	L2026M	WT	L2026M
AP26113	31 ± 15	39 ± 18	18 ± 3	17 ± 6
Crizotinib	45 ± 21	199 ± 39	25 ± 12	127 ± 44

Source: Squillace et al, 2013 AACR, #5655

LEERINK

CRIZOTINIB ACTIVITY IN ROS1+ PATIENTS SETS A HIGH BAR FOR RXDX-101 CLINICAL DEVELOPMENT

- Crizotinib Phase I/II data were convincing enough for some medical oncologists to use crizotinib off label in the NSCLC patients with ROS1 rearrangement.
- Data may be sufficient for a filing although PFE has not made a public announcement on regulatory strategy. Our KOLs considered a high likelihood of approval of crizotinib in the NSCLC patients with ROS1 rearrangement.
- The resistant profile for crizotinib treated ROS1 patients has not emerged and it is still unclear if the 2nd generation ALK inhibitors' robust activity against crizotinib resistant NSCLC shown in ALK+ patients still holds in the ROS1 rearrangement patients.
- Preclinical data showed some trend of better activity of RXDX-101 vs. crizotinib; however, RXDX-101 activity against crizotinib-resistant patients remains to be seen.

Source: Ou et al, 2013 ASCO, #8032

INVESTMENT CONSIDERATION #5

ALK INHIBITOR SPACE IS CROWDED

RXDX-101 – LIMITED MARKET POTENTIAL TARGETING ALK MUTATION

- Several 2nd generation ALK inhibitors are in late stage development
  - Potent activity against crizotinib resistant NSCLC patients
  - Various degree of capability to cross brain blood barrier (activity in NSCLC patients with brain metastases)
- Ceritinib (LDK378) from NVS is among the most promising candidates (breakthrough designation).
  - It has been evaluated in two Phase III trials in both front-line and crizotinib pretreated NSCLC.
  - NVS recently submitted an NDA filing for approval
- Alectinib (CH5424802) from Chugai/Roche was also granted breakthrough designation
  - Promising activity in both crizotinib naïve and resistant NSCLC patients
  - Impressive activity in NSCLC patients with brain mets – 16/20 (80%) NSCLC patients who had brain mets remained on study for over 6.6months.
- Crizotinib sales were only $280M in 2013
- RXDX-101 showed marginally better activity vs. crizotinib in preclinical studies, and clinical activity in crizotinib resistant patients remains to be seen

Source: Company Reports, publications and medical conference presentations

CROWDED SPACE OF SECOND GENERATION ALK INHIBITORS

Compound	Company	Development Stage	Indication	Activity	Activity in CNS	Reference
Ceritinib (LDK378)	NVS	Phase III, NDA submitted	NSCLC - Breakthrough Designation	58% (66/114) ORR (400-750mg/day) in all NSCLC pts, 57% (45/79) ORR in CRZ-pretreated, and 60% (21/35) in CRZ-naïve ALK+ NSCLC	Yes.	Shaw et al, ASCO 2013, #8010
Alectinib (CH5424802)	Chugai/ Roche	Phase I/II	NSCLC - Breakthrough Designation	94% (43/46) ORR (up to 300mg BID) vs. 50-61% for CRZ in CRZ-naïve ALK+ NSCLC; 54.5% in ALK+ crizotinib resistant NSCLC	Yes.	Seto et al, Lancet Oncol (2013) 14: 590-598; Ou et al, 2013 ESMO, #44
AP26113	ARIA	Phase I/II	NSCLC	75% (12/16) ORR (60-300mg/day) in CRZ-pretreated ALK+ NSCLC	Yes.	Camidage et al, ASCO 2013 , # 8031
TSR-011	TSRO	Phase I/II	NSCLC			
X-396	Xcovery	Phase I	NSCLC and other Advanced solid tumors			
P7170	Piramal Healthcare	Phase I	Solid tumors			
ASP3026	Astellas	Phase I	Advanced malignancies, B cell lymphoma, solid tumors			
GSK1838705	GSK	Pre clinical	NSCLC			
CEP-28122	Cephalon/ Teva	Pre clinical	Anaplastic large-cell lymphoma (ALCL), NSCLC, neuroblastoma cells			

Source: Company Reports, publications and medical conference presentations

RXDX-101 – PRECLINICAL DATA SUGGEST A PAN-TRK, ROS1 AND ALK INHIBITOR WITH POTENTIAL TO CROSS BBB

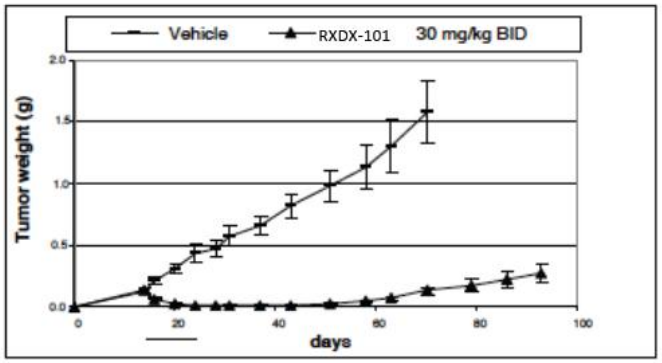
Target	TrkA	TrkB	TrkC	ROS1	ALK
IC50 (nM)	1	2	5	7	12

BBB penetration in 3 species (brain/blood ratio)	
Species	**Ratio**
Mouse	0.4
Rat	0.6-1.0
Dog	1.4-2.2

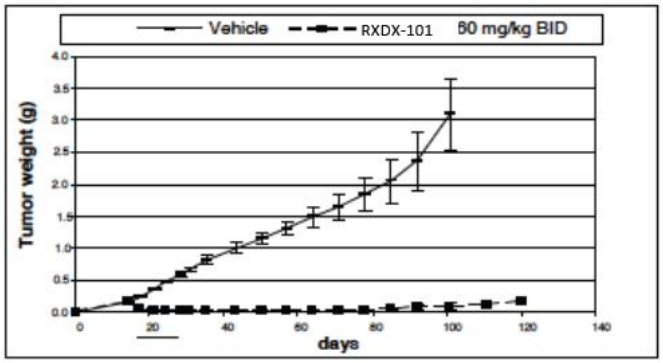
Source: Company Reports, Gainor et al, IASLC 2014,; Note: data as of Feb 18, 2014

RXDX-101 – PRECLINICAL ACTIVITY AGAINST ALK+ TUMORS

In vivo activity in ALK-driven NCI-H2228 non small cell lung cancer (NSCLC) mouse xenografts treated orally BID for 10 days

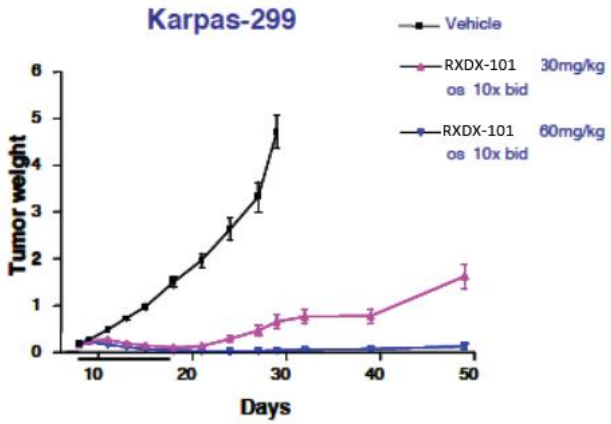


Tumor-free achieved in 2 out of 7 mice

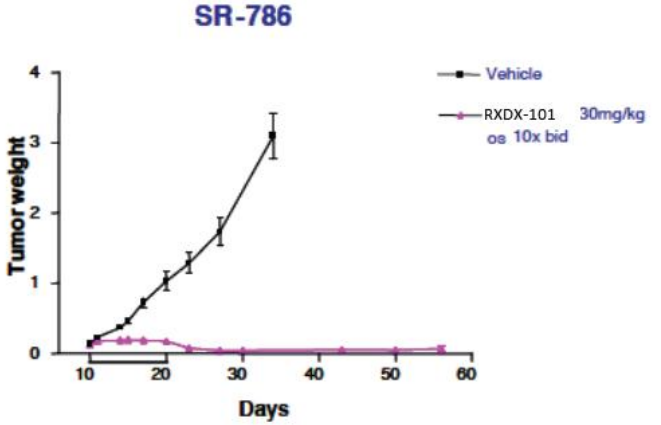


Tumor-free achieved in 5 out of 7 mice

In vivo activity in ALK-driven anaplastic large cell lymphoma (ALCL) mouse xenografts treated orally BID for 10 days



Tumor eradication in 4 out of 7 mice at day 90 (60 mg/kg)



Tumor eradication in 6 out of 7 mice at day 90

18

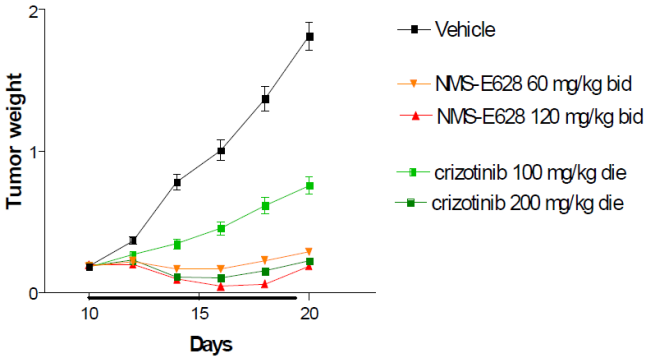
H2228 NSCLC cell line harbors an ALK rearrangement – NOT crizotinib resistant

Source: Company Reports

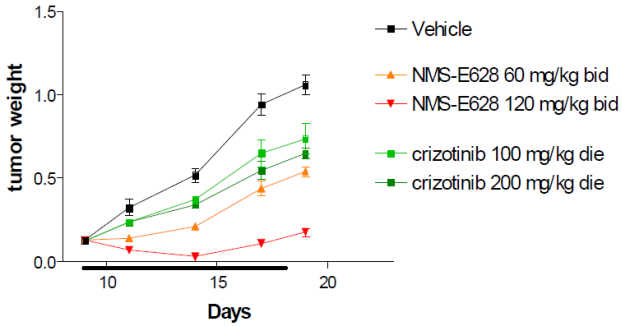
RXDX-101 PRECLINICAL DATA SHOWED MARGINAL IMPROVEMENT IN ALK+ ACTIVITY VS. CRIZOTINIB

ALK Inhibitors	Company	IC_{50} (μM)	IC_{50} (μM) (Ba/F3 TEL/ALK)					Stage of Development	NCT
		ALK	BA/F3	WT	L1196M	C1156Y	F1174L		
Crizotinib	PFE		2.4	0.45	1.9	1.5	1.4	Approved	NA
RXDX-101	RXDX	12	1.8	0.17	0.41	0.3	1.2	Phase I/II in TrkA, TrkB, TrkC, ROS1 and ALK	NCT02097810

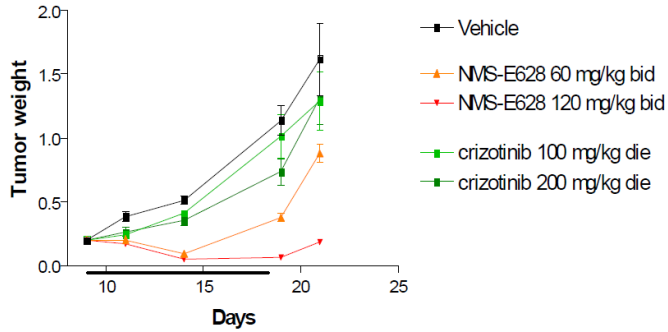
Ba/F3 ALK wt



Ba/F3 ALK L1196M



Ba/F3 ALK C1156Y



Source: Ardini et al, 2011 EORTC-NCI-AACR, #A232

OTHER ALK INHIBITORS SHOWED ROBUST PRECLINICAL ACTIVITY IN CRIZOTINIB-RESISTANT MUTATIONS

Ba/F3 cell line	AP26113	Crizotinib	ASP3026	CH5424802
Ba/F3 parental	4580 ± 1553	2065 ± 373	>10000	>10000
EML4-ALK	17 ± 4	137 ± 49	129 ± 21	15 ± 8
L1152R	17 ± 5	911 ± 136	5934 ± 2156	105 ± 35
G1269A	24 ± 4	798 ± 62	264 ± 65	103 ± 15
S1206Y	88 ± 3	509 ± 85	518 ± 74	58 ± 11
F1174L	95 ± 5	449 ± 117	978 ± 132	81 ± 4
L1196M	99 ± 21	870 ± 143	1902 ± 448	220 ± 49
D1203N	144 ± 8	693 ± 51	854 ± 164	85 ± 17
C1156Y	150 ± 9	2323 ± 117	2555 ± 86	194 ± 39
T1151T insertion	244 ± 16	1336 ± 490	5939 ± 2278	455 ± 143
G1202R	379 ± 68	874 ± 53	1856 ± 550	1009 ± 137

Activity tested in mutant EML4-ALK-driven cells

Source: Squillace et al, 2013 AACR, #5655

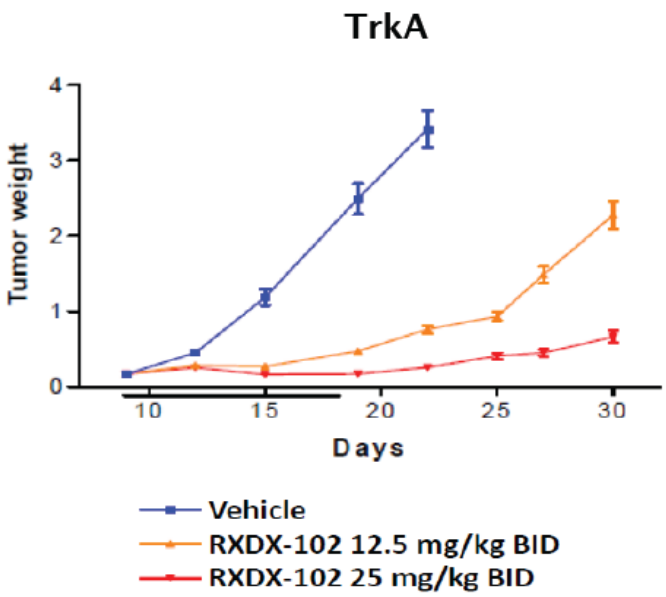
OTHER PIPELINE ASSETS

RXDX-102

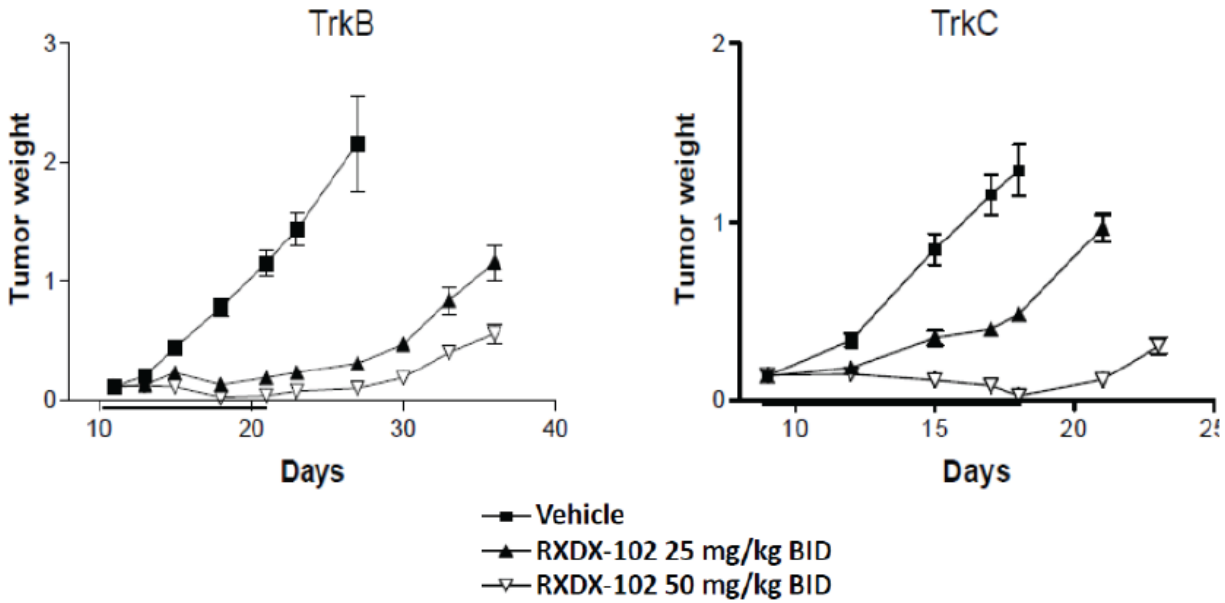
RXDX-102 IS A BACKUP ASSET TO RXDX-101

- RXDX-102 has different characteristics from RXDX-101
  - Less CNS penetration vs. RXDX-101
  - Less activity against ROS1 and ALK, a purer pan-Trk inhibitor

RXDX-102 was orally administered to nude mice bearing KM12 tumors



TrkB and TrkC-driven Ba/F3 cells were injected s.c. in SCID mice and animals were treated with RXDX-102



Source: Company Reports

INTELLECTUAL PROPERTY

RXDX-101 AND RXDX-102 – INTELLECTUAL PROPERTY

- RXDX-101
  - Compound claims, composition claims and claims to a method of manufacturing
  - US patent No. 8,299,057
  - Expiry of 2029
  - Related international patents have been issued in New Zealand, South Africa, Ukraine, application pending in Europe and other countries.

- RXDX-102
  - Compound claims, composition claims and claims to a method of manufacturing
  - US patent No. 8,114,865
  - Expiry of 2028
  - Related international patents have been issued in Japan and Mexico, application pending in Europe and other countries.

FINANCIALS

INCOME STATEMENT

RXDX - Income Statement ($000, except per share value)	2012A	2013A	Mar-14E	Jun-14E	Sep-14E	Dec-14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
RXDX-101 sales - US							0	0	0	0	8,471	58,747	91,672
% to RXDX							*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*
RXDX-101 sales - Ex-US							0	0	0	0	0	21,173	95,033
% to RXDX							*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*
Total revenue	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**7,793**	**73,526**	**171,769**
COGS	0	0	0	0	0	0	0	0	0	0	678	6,394	14,936
% gross margin							*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*
growth q/q													
R&D	708	10,171	4,500	4,950	5,940	6,534	21,924	33,357	46,699	56,039	56,039	54,358	52,727
% growth q/q			*10%*	*10%*	*20%*	*10%*	*116%*	*52%*	*40%*	*20%*	*0%*	*-3%*	*-3%*
SG&A	548	3,731	2,000	2,200	2,640	2,904	9,744	14,825	16,308	32,615	48,923	53,816	56,506
% growth q/q			*10%*	*10%*	*20%*	*10%*	*161%*	*52%*	*10%*	*100%*	*50%*	*10%*	*5%*
% of revenue											*628%*	*73%*	*33%*
Total expenses	**1,256**	**13,902**	**6,500**	**7,150**	**8,580**	**9,438**	**31,668**	**48,182**	**63,007**	**88,655**	**105,640**	**114,567**	**124,170**
Operating Income	**(1,256)**	**(13,902)**	**(6,500)**	**(7,150)**	**(8,580)**	**(9,438)**	**(31,668)**	**(48,182)**	**(63,007)**	**(88,655)**	**(97,847)**	**(41,041)**	**47,599**
Other income (expenses)	0	(106)	0	0	0	0	0	0	0	0	0	0	0
Interest income (expenses)	(23)	(204)											
Tax	1	2	0	0	0	0	0	0					
% Tax rate	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
Net income to common shares	**(1,280)**	**(14,214)**	**(6,500)**	**(7,150)**	**(8,580)**	**(9,438)**	**(31,668)**	**(48,182)**	**(63,007)**	**(88,655)**	**(97,847)**	**(41,041)**	**47,599**
EPS - basic	**(2.00)**	**(3.83)**	**(0.33)**	**(0.36)**	**(0.43)**	**(0.47)**	**(1.61)**	**(1.92)**	**(2.08)**	**(2.20)**	**(2.02)**	**(0.85)**	**0.98**
EPS - dilutive	**(2.00)**	**(3.83)**	**(0.33)**	**(0.36)**	**(0.43)**	**(0.47)**	**(1.61)**	**(1.92)**	**(2.08)**	**(2.20)**	**(2.02)**	**(0.85)**	**0.95**
Basic shares	640	3,712	19,575	19,673	19,771	19,870	19,722	25,132	30,351	40,381	48,422	48,470	48,519
Dilutive shares	640	3,712	21,260	21,362	21,463	21,566	21,413	26,836	32,062	42,094	50,136	50,186	50,236

Source: Company Reports and Leerink Partners

MARKET MODEL - TRK

NSCLC Market Model - Trk / ROS1	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
NSCLC market - US - Trk																		
NSCLC incidence - US	190,579	192,484	194,409	196,353	198,317	200,300	202,303	204,326	206,369	208,433	210,517	212,622	214,749	216,896	219,065	221,256	223,468	225,703
% growth y/y	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
% pts has Trk rearrangement	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
NSCLC pts with Trk rearrangement	1,906	1,925	1,944	1,964	1,983	2,003	2,023	2,043	2,064	2,084	2,105	2,126	2,147	2,169	2,191	2,213	2,235	2,257
% treated with RXDX-101	*0%*	*0%*	*0%*	*0%*	*3%*	*23%*	*33%*	*43%*	*48%*	*48%*	*48%*	*48%*	*48%*	*48%*	*48%*	*48%*	*48%*	*48%*
# patients treated	0	0	0	0	59	461	668	879	991	1,000	1,010	1,021	1,031	1,041	1,052	1,062	1,073	1,083
Cost per month	12,650	13,030	13,420	13,823	14,238	14,665	15,105	15,558	16,025	16,505	17,001	17,511	18,036	18,577	19,134	19,708	20,300	20,909
% growth	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*
Treatment duration	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Cost per course	101,200	104,236	107,363	110,584	113,901	117,319	120,838	124,463	128,197	132,043	136,004	140,084	144,287	148,616	153,074	157,666	162,396	167,268
RXDX-101 sales	0	0	0	0	6,777	54,047	80,671	109,354	126,989	132,106	137,430	142,968	148,730	154,724	160,959	167,446	174,194	181,214
% Probability of success	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
RXDX-101 sales - US - PW - Trk	**0**	**0**	**0**	**0**	**3,388**	**27,024**	**40,336**	**54,677**	**63,494**	**66,053**	**68,715**	**71,484**	**74,365**	**77,362**	**80,480**	**83,723**	**87,097**	**90,607**
NSCLC market - EU-27 - Trk																		
NSCLC incidence - EU-27	348,500	351,985	355,505	359,060	362,650	366,277	369,940	373,639	377,376	381,149	384,961	388,810	392,699	396,626	400,592	404,598	408,644	412,730
% growth y/y	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
% pts has Trk rearrangement	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
NSCLC pts with Trk rearrangement	3,485	3,520	3,555	3,591	3,627	3,663	3,699	3,736	3,774	3,811	3,850	3,888	3,927	3,966	4,006	4,046	4,086	4,127
% treated with RXDX-101	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*25%*	*40%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*	*45%*
# patients treated	0	0	0	0	0	183	925	1,495	1,698	1,715	1,732	1,750	1,767	1,785	1,803	1,821	1,839	1,857
Cost per month	11,000	11,110	11,221	11,333	11,447	11,561	11,677	11,793	11,911	12,031	12,151	12,272	12,395	12,519	12,644	12,771	12,898	13,027
% growth	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
Treatment duration	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Cost per course	88,000	88,880	89,769	90,666	91,573	92,489	93,414	94,348	95,291	96,244	97,207	98,179	99,161	100,152	101,154	102,165	103,187	104,219
RXDX-101 sales	0	0	0	0	0	16,938	86,394	141,008	161,823	165,076	168,394	171,778	175,231	178,753	182,346	186,011	189,750	193,564
% Probability of success	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
RXDX-101 sales - EU-27 - PW - Trk	**0**	**0**	**0**	**0**	**0**	**8,469**	**43,197**	**70,504**	**80,911**	**82,538**	**84,197**	**85,889**	**87,615**	**89,377**	**91,173**	**93,006**	**94,875**	**96,782**

Source: Company Reports and Leerink Partners

MARKET MODEL – ROS1

NSCLC Market Model - Trk / ROS1	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
NSCLC market - US - ROS1																		
NSCLC incidence - US	190,579	192,484	194,409	196,353	198,317	200,300	202,303	204,326	206,369	208,433	210,517	212,622	214,749	216,896	219,065	221,256	223,468	225,703
% growth y/y	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
% pts has ROS1 rearrangement	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*
NSCLC pts with ROS1 rearrangement	2,859	2,887	2,916	2,945	2,975	3,004	3,035	3,065	3,096	3,126	3,158	3,189	3,221	3,253	3,286	3,319	3,352	3,386
% treated with RXDX-101	*0%*	*0%*	*0%*	*0%*	*3%*	*18%*	*28%*	*33%*	*36%*	*36%*	*36%*	*36%*	*36%*	*36%*	*36%*	*36%*	*36%*	*36%*
# patients treated	0	0	0	0	89	541	850	1,011	1,114	1,126	1,137	1,148	1,160	1,171	1,183	1,195	1,207	1,219
Cost per month	12,650	13,030	13,420	13,823	14,238	14,665	15,105	15,558	16,025	16,505	17,001	17,511	18,036	18,577	19,134	19,708	20,300	20,909
% growth	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*	*3%*
Treatment duration	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Cost per course	101,200	104,236	107,363	110,584	113,901	117,319	120,838	124,463	128,197	132,043	136,004	140,084	144,287	148,616	153,074	157,666	162,396	167,268
RXDX-101 sales	0	0	0	0	10,165	63,447	102,673	125,884	142,862	148,619	154,609	160,840	167,321	174,064	181,079	188,377	195,968	203,866
% Probability of success	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
RXDX-101 sales - US - PW - ROS1	**0**	**0**	**0**	**0**	**5,082**	**31,724**	**51,336**	**62,942**	**71,431**	**74,310**	**77,304**	**80,420**	**83,661**	**87,032**	**90,540**	**94,188**	**97,984**	**101,933**
NSCLC market - EU-27 - ROS1																		
NSCLC incidence - EU-27	348,500	351,985	355,505	359,060	362,650	366,277	369,940	373,639	377,376	381,149	384,961	388,810	392,699	396,626	400,592	404,598	408,644	412,730
% growth y/y	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
% pts has ROS1 rearrangement	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*	*1.5%*
NSCLC pts with ROS1 rearrangement	5,228	5,280	5,333	5,386	5,440	5,494	5,549	5,605	5,661	5,717	5,774	5,832	5,890	5,949	6,009	6,069	6,130	6,191
% treated with RXDX-101	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*20%*	*25%*	*30%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*	*33%*
# patients treated	0	0	0	0	0	275	1,110	1,401	1,698	1,887	1,906	1,925	1,944	1,963	1,983	2,003	2,023	2,043
Cost per month	11,000	11,110	11,221	11,333	11,447	11,561	11,677	11,793	11,911	12,031	12,151	12,272	12,395	12,519	12,644	12,771	12,898	13,027
% growth	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
Treatment duration	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
Cost per course	88,000	88,880	89,769	90,666	91,573	92,489	93,414	94,348	95,291	96,244	97,207	98,179	99,161	100,152	101,154	102,165	103,187	104,219
RXDX-101 sales	0	0	0	0	0	25,407	103,672	132,195	161,823	181,583	185,233	188,956	192,754	196,628	200,581	204,612	208,725	212,920
% Probability of success	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
RXDX-101 sales - EU-27 - PW	**0**	**0**	**0**	**0**	**0**	**12,704**	**51,836**	**66,098**	**80,911**	**90,792**	**92,616**	**94,478**	**96,377**	**98,314**	**100,290**	**102,306**	**104,363**	**106,460**
RXDX-101 sales - US - Trk/ROS1	**0**	**0**	**0**	**0**	**8,471**	**58,747**	**91,672**	**117,619**	**134,925**	**140,363**	**146,019**	**151,904**	**158,026**	**164,394**	**171,019**	**177,911**	**185,081**	**192,540**
RXDX-101 sales - EU-27 - Trk/ROS1	**0**	**0**	**0**	**0**	**0**	**21,173**	**95,033**	**136,602**	**161,823**	**173,329**	**176,813**	**180,367**	**183,993**	**187,691**	**191,463**	**195,312**	**199,238**	**203,242**

Source: Company Reports and Leerink Partners

RXDX-101 DCF VALUATION

DCF Valuation	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
RXDX-101 US sales - NSCLC	0	0	0	0	8,471	58,747	91,672	117,619	134,925	140,363	146,019	151,904	158,026	164,394	171,019	177,911	185,081	192,540
Total RXDX-101 US sales	**0**	**0**	**0**	**0**	**8,471**	**58,747**	**91,672**	**117,619**	**134,925**	**140,363**	**146,019**	**151,904**	**158,026**	**164,394**	**171,019**	**177,911**	**185,081**	**192,540**
% to RXDX	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*
RXDX-101 Ex-US sales - NSCLC	0	0	0	0	0	21,173	95,033	136,602	161,823	173,329	176,813	180,367	183,993	187,691	191,463	195,312	199,238	203,242
Total RXDX-101 Ex-US sales	**0**	**0**	**0**	**0**	**0**	**21,173**	**95,033**	**136,602**	**161,823**	**173,329**	**176,813**	**180,367**	**183,993**	**187,691**	**191,463**	**195,312**	**199,238**	**203,242**
% Ex-US royalty to RXDX	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*	*92%*
Total revenues	**0**	**0**	**0**	**0**	**7,793**	**73,526**	**171,769**	**233,883**	**273,008**	**288,597**	**297,006**	**305,689**	**314,657**	**323,918**	**333,484**	**343,365**	**353,573**	**364,120**
COGS	0	0	0	0	678	6,394	14,936	20,338	23,740	25,095	25,827	26,582	27,361	28,167	28,999	29,858	30,745	31,663
% of US revenue	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*	*8%*
R&D	21,924	33,357	46,699	56,039	56,039	54,358	52,727											
SG&A (related to 101 marketing)	9,744	14,825	16,308	32,615	48,923	53,816	56,506	59,332	62,298	65,413	68,684	70,744	72,867	75,053	77,304	79,623	82,012	84,472
Milestone to Nerviano					(55,000)	(20,000)	(20,000)	(10,000)										
Operating income	(31,668)	(48,182)	(63,007)	(88,655)	(152,847)	(61,041)	27,599	144,214	186,970	198,088	202,496	208,364	214,429	220,699	227,181	233,884	240,816	247,985
Tax										69,331	70,873	72,927	75,050	77,245	79,513	81,859	84,286	86,795
% tax										*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
Net income	(31,668)	(48,182)	(63,007)	(88,655)	(152,847)	(61,041)	27,599	144,214	186,970	128,757	131,622	135,436	139,379	143,454	147,668	152,025	156,530	161,190
Period	0.00	0.73	1.73	2.73	3.73	4.73	5.73	6.73	7.73	8.73	9.73	10.73	11.73	12.73	13.73	14.73	15.73	16.73
DCF	**(31,668)**	**(44,937)**	**(53,422)**	**(68,334)**	**(107,103)**	**(38,884)**	**15,983**	**75,923**	**89,484**	**56,021**	**52,061**	**48,700**	**45,561**	**42,631**	**39,893**	**37,337**	**34,949**	**32,717**

DCF	159,246
Cash	97,183
Pipeline	40,000
Total valuation	296,429
Value per share	**$13.75**
Share (2014)	21,566
Discount rate	10%

Source: Leerink Partners

MANAGEMENT

MANAGEMENT

Name/Title	Previous Experience
Jonathan Lim, M.D. Chairman, CEO, and Co-Founder	Former Chair, CEO of Eclipse; Former President, CEO, Director at Halozyme; McKinsey; NIH Postdoc Fellow at Harvard; surgical resident at NYH-Cornell
Sara Zaknoen, M.D. Chief Medical Officer	Former CMO at Polynoma, Tragara and Cabrellis; oncology senior leadership roles at Novartis and Schering-Plough; trained hematologist/oncologist
Zachary Hornby CFO and VP, Corporate Development	Former Senior Director of Business Development at Fate Therapeutics; Director of BD at Halozyme; L.E.K. Consulting; Harvard Business School
Tony Shuber Chief Technology Officer	Former CTO and Co-Founder of Predictive Biosciences; EVP, CTO and Co-Founder of EXACT Sciences; Genzyme Genetics; Genetics Institute
Matt Onaitis General Counsel and Secretary	Former General Counsel at Trius and Somaxon; Associate General Counsel at Biogen Idec; Director of Legal Affairs at Elan Corporation, plc; Stanford Law School

Source: Company reports

RXDX - Income Statement ($000, except per share value)	2012A	2013A	Mar-14E	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
% gross margin							*8%*	*8%*	*8%*	*8%*	*8%*	*8%*
growth q/q												
R&D	708	10,171	4,500	4,950	5,940	6,534	21,924	33,357	46,699	56,039	56,039	54,358
% growth q/q			*10%*	*10%*	*20%*	*10%*	*116%*	*52%*	*40%*	*20%*	*0%*	*-3%*
SG&A	548	3,731	2,000	2,200	2,640	2,904	9,744	14,825	16,308	32,615	48,923	53,816
% growth q/q			*10%*	*10%*	*20%*	*10%*	*161%*	*52%*	*10%*	*100%*	*50%*	*10%*
% of revenue											*628%*	*73%*
Total expenses	**1,256**	**13,902**	**6,500**	**7,150**	**8,580**	**9,438**	**31,668**	**48,182**	**63,007**	**88,655**	**105,640**	**114,567**
Operating Income	**(1,256)**	**(13,902)**	**(6,500)**	**(7,150)**	**(8,580)**	**(9,438)**	**(31,668)**	**(48,182)**	**(63,007)**	**(88,655)**	**(97,847)**	**(41,041)**
Other income (expenses)	0	(106)	0	0	0	0	0	0	0	0	0	0
Interest income (expenses)	(23)	(204)										
Tax	1	2	0	0	0	0	0	0				
% Tax rate	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
Net income to common shares	**(1,280)**	**(14,214)**	**(6,500)**	**(7,150)**	**(8,580)**	**(9,438)**	**(31,668)**	**(48,182)**	**(63,007)**	**(88,655)**	**(97,847)**	**(41,041)**
EPS - basic	**(2.00)**	**(3.83)**	**(0.33)**	**(0.36)**	**(0.43)**	**(0.47)**	**(1.61)**	**(1.92)**	**(2.08)**	**(2.20)**	**(2.02)**	**(0.85)**
EPS - dilutive	**(2.00)**	**(3.83)**	**(0.33)**	**(0.36)**	**(0.43)**	**(0.47)**	**(1.61)**	**(1.92)**	**(2.08)**	**(2.20)**	**(2.02)**	**(0.85)**
Basic shares	640	3,712	19,575	19,673	19,771	19,870	19,722	25,132	30,351	40,381	48,422	48,470
Dilutive shares	640	3,712	21,260	21,362	21,463	21,566	21,413	26,836	32,062	42,094	50,136	50,186

Sources: Company Reports, Leerink Partners

Disclosures Appendix

Analyst Certification

I, Howard Liang, Ph.D., 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.

Distribution of Ratings/Investment Banking Services (IB) as of 03/31/14				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	131	68.23	46	35.11
HOLD [MP]	61	31.77	3	4.92
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.

Important Disclosures

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