COWEN
AND COMPANY

Biotechnology

Loxo Oncology

Equity Research

Initiating Coverage

September 2, 2014

Price: $13.01 (09/1/2014)
Price Target: NA

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: LOXO
52-Week Range:	$13.42 - 12.69
Market Cap (MM):	$207.4
Net Debt (MM):	$(15.0)
Cash/Share:	$51.73
Dil. Shares Out (MM):	15.9
Enterprise Value (MM):	$220.3
ROIC:	NA
ROE (LTM):	NA
BV/Share:	$(35.30)
Dividend:	NA

FY (Dec)	2014E	2015E	2016E
Earnings Per Share			
Q1	$(1.06)A	$(0.50)	-
Q2	$(1.93)	$(0.51)	-
Q3	$(0.47)	$(0.51)	-
Q4	$(0.50)	$(0.52)	-
Year	$(2.55)	$(2.05)	$0.15
P/E	NM	NM	86.7x
Revenue (MM)			
Year	$0.0	$0.0	$50.0
EV/S	-	-	4.4x

Initiation: Tracking New Paths In Oncology

The Cowen Insight

We are initiating coverage of Loxo Oncology with an Outperform rating. Loxo seeks to develop targeted, small molecule drugs for patients with genetically-defined cancers. Lead candidate LOXO-101 is a TRK inhibitor ("track" inhibitor) in Phase I development with $200MM+ U.S. sales potential in lung cancer. We expect LOXO shares to appreciate as this and other pipeline candidates advance.

Selective Drugs For Selected Cancers

Loxo seeks to develop highly specific inhibitors of oncogenes that are selectively activated in subpopulations of cancer patients. Drugs like Gleevec in CML, Tarceva and Xalkori in lung cancer, and Zelboraf in melanoma have established a successful precedent for this strategy. Loxo's drug candidates are sourced from a discovery collaboration with Array Biopharma, and are being directed against various validated and emerging cancer targets. Benefits of Loxo's business model include a capital efficient means for pipeline creation, the potential to generate early proof-of-concept efficacy, and the ability to take advantage of an abbreviated FDA approval pathway for targeted cancer drugs.

LOXO-101: A Potential Best In Class TRK Inhibitor

Tropomyosin Receptor Kinase (TRK) family consists of three tyrosine kinases (TRKA, TRKB, and TRKC) that have been implicated in driving a subset of lung, colorectal, breast, salivary, and other solid tumors. LOXO-101 is a highly selective (>38-fold) inhibitor of the TRK family that does not cross the blood brain barrier, thus reducing the potential for on-target adverse effects. In April 2014, Loxo began a Phase Ia dose escalation study in all-comers solid tumor patients with the goal of rapidly identifying an optimal dose. Beginning in Q2:15, a multi-arm Phase Ib trial will investigate LOXO-101's activity in various patient subsets selected for TRK alterations. While a dearth of information on the frequency of TRK alterations in various tumor types makes it difficult to estimate LOXO-101's commercial potential, we think the drug could achieve U.S. sales of >$200MM in lung cancer alone based upon the assumptions that (1) 1-4% of all non-squamous patients might be eligible for therapy and (2) LOXO-101 is priced at $125K per course of therapy.

Valuation Leaves Much Room For Upside

Loxo raised $64MM in a July IPO and is financed through 2016, including through potential proof-of-concept data on LOXO-101. Based on LOXO-101's opportunity in lung cancer ($12.50 on an NPV basis) and the company's net cash position ($7.27/share), we view LOXO shares as approximately 50% undervalued relative to the market. Additional upside could be associated with the successful development of LOXO-101 in additional tumor subpopulations or the advancement of other pipeline candidates.

At A Glance

Our Investment Thesis

Factors that support our positive investment opinion on LOXO shares include (1) the company's focus on targeted therapeutics for cancer, an area of medicine we find compelling; (2) an efficient R&D strategy that features the potential for early confirmation of efficacy; (3) a modest valuation that should permit plenty of upside in the event of success; and (4) a credible and experienced management team. We expect LOXO shares to appreciate as LOXO-101 and other pipeline candidates advance.

Forthcoming Catalysts

- Phase Ia dose-escalation data on LOXO-101 in solid tumors (H1:15)
- Initiate Phase Ib trial on LOXO-101 in patients with TRK-driven tumors (Q2:15)
- Advance companion diagnostic for LOXO-101 (2015)
- File IND for LOXO-200 (undisclosed oncology target) (YE:15)
- Data from Phase Ib LOXO-101 expansion cohorts (Late 2015/Early 2016)

Base Case Assumptions

- LOXO-101 successfully developed for the treatment of TRK+ NSCLC patients
- No LOXO-101 sales until 2019
- Secure ex-U.S. partner for LOXO-101

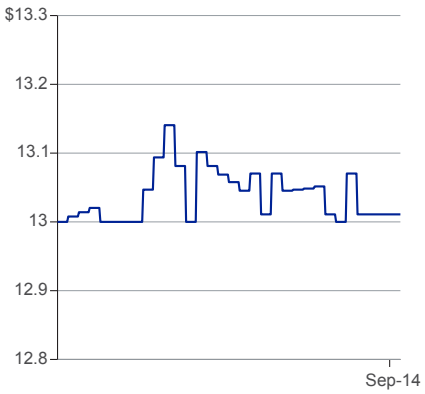
Upside Scenario

- Successful development of LOXO-101 in additional indications
- Higher than expected prevalence of TRK mutations in NSCLC and other tumor types

Downside Scenario

- Clinical setbacks in the ongoing Phase I trial of LOXO-101
- Lower than expected prevalence of TRK mutations in NSCLC and other tumor types
- Competing TRK inhibitors including Ignyta's RXDX-101 have superior properties

Price Performance



Source: Bloomberg

Company Description

Loxo Oncology is an early-stage company focused on the development of targeted therapeutics for patients with genetically defined cancers. Loxo was founded with the goal of combining novel biological insights, leading chemistry, and clinical development expertise to rapidly and efficiently develop small molecule drug candidates for targeted cancer subpopulations. Lead compound LOXO-101 is an inhibitor of the Tropomyosin Receptor Kinase (TRK) family, and is being evaluated in Phase I studies that could produce proof-of-concept efficacy data within the next 12-18 months. Loxo is using its Scientific Advisory Board (SAB) to identify other interesting oncology targets, and is deploying a collaboration with Array Biopharma to create a pipeline of up to five additional clinical candidates. The company was founded in 2013 and is headquartered in Stamford, CT.

Analyst Top Picks

	Ticker	Price (09/1/2014)	Price Target	Rating
Sunesis Pharmaceuticals	SNSS	$7.49	$NA	Outperform
bluebird bio	BLUE	$40.01	$NA	Outperform
Relypsa	RLYP	$25.28	$NA	Outperform

Investment Summary

Loxo Oncology is an early-stage biotechnology company focused on the development of targeted therapeutics for patients with genetically defined cancers. Loxo was founded with the goal of combining novel biological insights, leading chemistry, and clinical development expertise to rapidly and efficiently develop small molecule drug candidates for targeted cancer subpopulations. Lead compound LOXO-101 is an inhibitor of the Tropomyosin Receptor Kinase (TRK) family, which consists of three transmembrane tyrosine kinases (TRKA, TRKB, and TRKC) that have been implicated in driving a subset of lung, colorectal, breast, salivary, and other solid tumors. LOXO-101 is being evaluated in Phase I studies that could produce proof-of-concept efficacy data within the next 12-18 months. While a dearth of information on the frequency of TRK alterations in various tumor types makes it difficult to estimate LOXO-101's potential market opportunity, we think the drug could achieve U.S. sales of >$200MM in lung cancer alone. Loxo is using its Scientific Advisory Board (SAB) to identify other interesting oncology targets, and is deploying a collaboration with Array Biopharma (ARRY, not rated) to create a pipeline of up to five additional clinical candidates. The company expects to file its next IND on an as yet undisclosed target in H2:15.

Loxo Oncology's Pipeline

Therapeutic Class/Product	Indication	P-C	I	II	III	FILING	MKT	Comments
Oncology								
LOXO-101	TRK driven tumors		▪					Phase Ia dose escalation trial began in April 2014
LOXO-200	Oncology	▪						IND expected in late 2015
LOXO-300	Oncology	▪						Under development with Array BioPharma
Undisclosed candidate #4	Oncology	▪						Under development with Array BioPharma
Undisclosed candidate #5	Oncology	▪						Under development with Array BioPharma
Undisclosed candidate #6	Oncology	▪						Option to license one additional program via Array collaboration
Total Drugs In Development		**5**	**1**	**0**	**0**	**0**	**0**	
Stamford, CT	**Investor Relations Contact: Jake Van Naarden (203) 653-3883**							

Source: Cowen and Company

Combining Biology, Chemistry, And Clinical Expertise To Accelerate Drug Discovery

Loxo's singular focus lies in developing selective, potent, targeted small molecules that inhibit pathways known to be activated in various tumors. There is now abundant evidence that certain cancers can be "driven" to grow out of control by the activation of a particular oncogene (e.g. BCR-ABL in CML, EGFR and ALK in lung cancer, BRAF in melanoma). Tumors that rely on a single, dominant oncogene for growth are termed "oncogene addicted". Moreover, there is plenty of precedent to indicate that drugs that inhibit signaling in oncogene addicted tumors can have a meaningful impact on

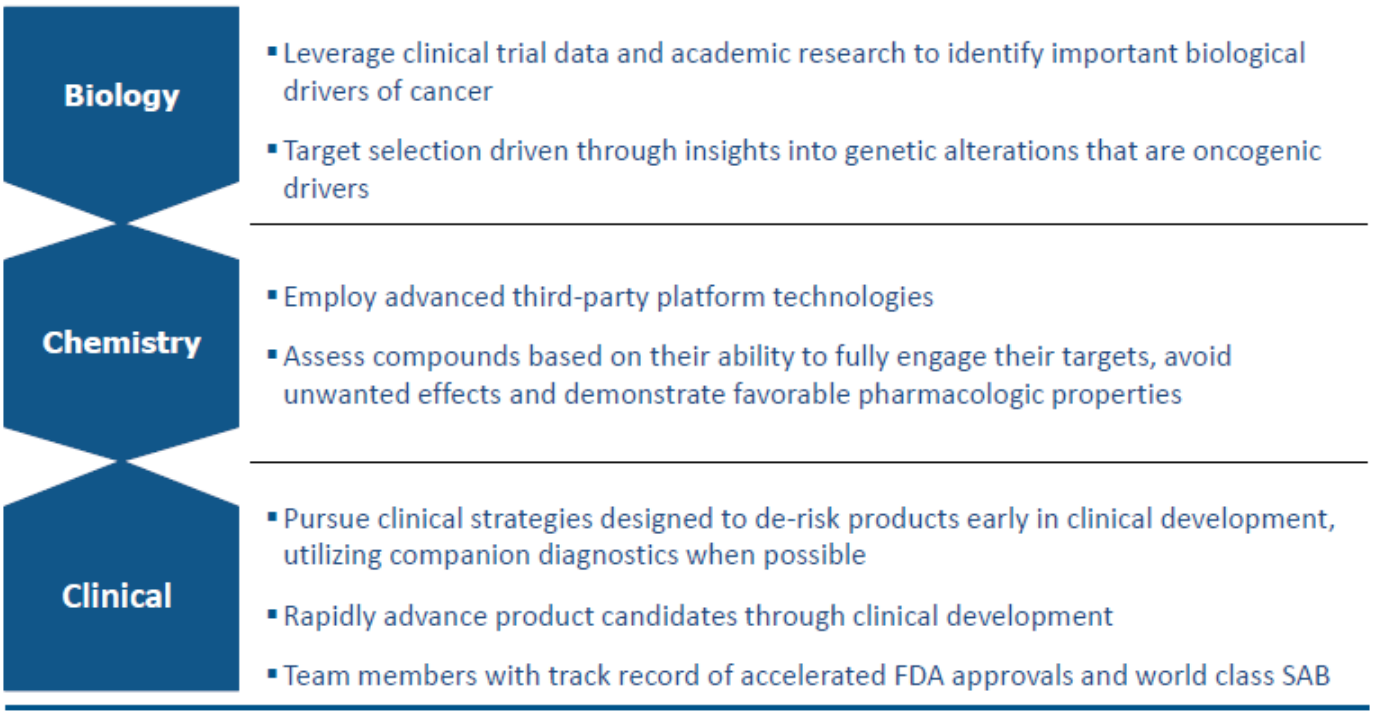
patient outcomes (Gleevec in CML, Tarceva in NSCLC, Xalkori in NSCLC, Zelboraf in melanoma). Loxo is hoping to pursue this now well established drug development paradigm by developing a pipeline of compounds than inhibit known as well as novel oncogene targets. While competition in this field in intense, an efficient strategy should allow Loxo to compete effectively in a field that features a growing number of drug development opportunities.

Biology. The selection of a biologically validated target is critical to the success of any selective approach in oncology. Loxo works closely with academic institutions and a renowned SAB to identify promising novel targets as early as possible. The company also uses these resources to prioritize targets that have already been validated, but lack optimal therapeutic interventions.

Chemistry. Loxo seeks only highly potent and selective inhibitors with favorable pharmacologic properties. The company has outsourced compound generation and lead optimization to Array BioPharma via a multi-year, multi-target drug discovery collaboration.

Clinical Development. Developing highly targeted drugs for selected cancer populations should allow Loxo to generate proof-of-concept efficacy data quickly, discontinue less promising candidates early on, and conduct abbreviated pivotal trials (possibly single arm in nature) in support of rapid FDA approval. The Loxo team has much clinical development and regulatory experience in oncology.

The Loxo Approach To Oncology Drug Development



Source: Loxo Oncology

LOXO-101 "On Track" For Early Proof-Of-Concept

Lead candidate LOXO-101 is a small molecule pan-inhibitor of the TRKA, TRKB, and TRKC receptor tyrosine kinases. LOXO-101 was discovered at Array BioPharma, and was initially being pursued as a pain drug based upon the known role of TRKA (the natural receptor for nerve growth factor) in sensory neurons. However, in late 2012 it was discovered that TRK translocations played a role in driving a small percent of non-small cell lung cancers. Shortly afterward, Loxo was able to obtain worldwide rights to the candidate in return for modest milestones and single digit royalties. LOXO-101 is both highly potent (low nM) and specific (at least 38-fold selective) for the TRKA, TRKB, and TRKC kinases. Loxo began a Phase Ia dose escalation study in April 2014 in all-comers solid tumor patients in order to allow for rapid dose escalation into a potentially therapeutically active range. The drug is dosed orally BID or QD over a 28 day cycle. Loxo has reported that LOXO-101 has been safe and well tolerated in the initial dose cohort with good tolerability, and that dosing in the second cohort is ongoing. Centers participating in the study do have the ability to genotype patients, and the option to direct any patients with TRK driver alterations to this study. Hence it is possible this trial could produce early indications of activity. Following selection of an optimal dose, Loxo will begin enrolling a multi-arm Phase Ib trial that will investigate LOXO-101's activity in various patient subsets selected for TRK alterations. We would expect this trial to better define the drug's efficacy profile.

Estimating LOXO-101's Commercial Opportunity

The role played by TRK in cancerous growth represents a relatively new discovery, and few studies have sought to quantify the incidence of TRK gene alterations. While there is some evidence to suggest that TRK alterations contribute to tumor growth across multiple histologies, we have based our model upon the lung cancer opportunity where at least one published study suggests that 1-4% of all non-squamous tumors might be driven by TRK alterations. Assuming an incidence toward the midpoint of this range (2%), an initial price of $125,000 per course of therapy, and a fairly high penetration of this market (70-75%), we estimate U.S. sales of LOXO-101 in lung might exceed $200MM by 2024. We view the rest of world market as a similarly sized opportunity. LOXO-101 is protected by a U.S. composition of matter patent that expires in 2029.

LOXO-101's NSCLC Market Opportunity: TRK Alteration Sensitivity Analysis

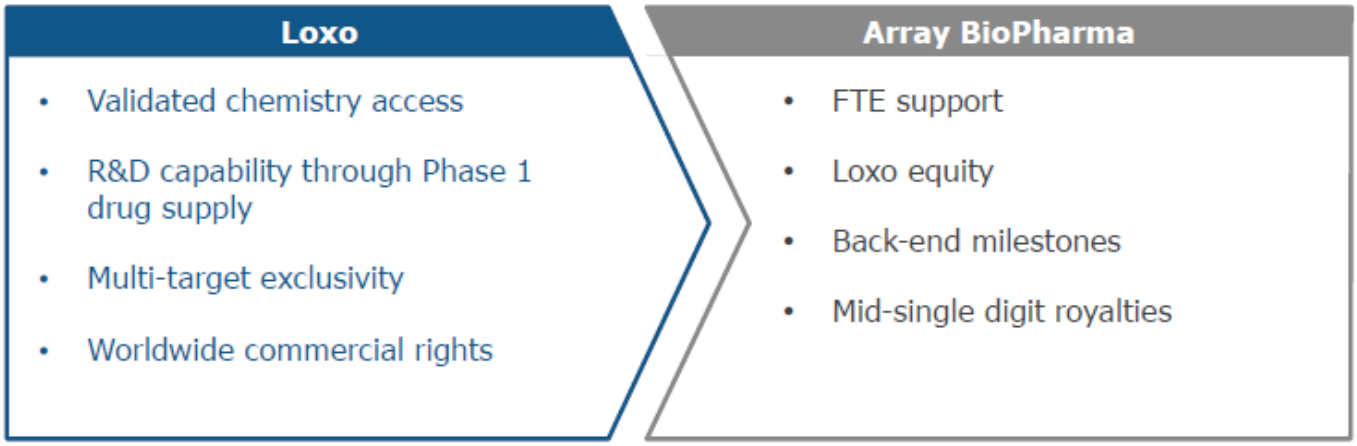
NSCLC Market Opportunity (US)	Low-end	Mid-end	High-end
# of Lung Cancer patients (US 2014 incidence)	224,000	224,000	224,000
% of pts with NSCLC	*85%*	*85%*	*85%*
# of NSCLC patients (US 2014 incidence)	190,400	190,400	190,400
% of patients with non-squamous cell carcinoma	*75%*	*75%*	*75%*
# of patients with non-squamous cell carcinoma	142,800	142,800	142,800
% of pts with Stage III/IV NSCLC	*80%*	*80%*	*80%*
# of pts with Stage III/IV NSCLC	114,240	114,240	114,240
% of pts eligible for chemotherapy	*75%*	*75%*	*75%*
# of pts eligible for Chemotherapy	85,680	85,680	85,680
% of pts with TRK driver alterations	*1%*	*2%*	*4%*
# of pts with TRK alterations	857	1,714	3,427
Cost of treatment/patient	*$125,000*	*$135,000*	*$150,000*
Total U.S. Market ($MM)	**$107**	**$231**	**$514**

Source: Cowen and Company

Array Deal Provides The Pipeline

In July 2013, Loxo signed a collaboration with Array Biopharma to discover up to five additional small molecule drug candidates, excluding LOXO-101. Under this collaboration, Loxo and Array have identified 12 oncology targets that are being assessed for chemical tractability and clinical utility. By January 2015, these targets will be narrowed down to six targets, which by October 2015 will be further prioritized to 4 lead programs, and an option on a fifth program. Array will be responsible for compound discovery, lead generation and optimization, IND enabling studies, and drug supply through Phase I studies. In return, Loxo will provide Array with FTE support, milestones, and a mid-single digit royalty on future sales. Array was also granted a ~10% equity position in Loxo. We view Array as a high quality chemistry platform that should provide interesting candidates to Loxo for several years on a cost efficient basis.

Array BioPharma Collaboration Agreement



Source: Loxo Oncology

Making The Investment Case For LOXO Shares

Loxo Oncology completed an IPO in July raising net proceeds of approximately $64MM. Inclusive of $51MM in pre-IPO cash, the company's pro forma cash balance as of June 30 was approximately $116MM. We believe Loxo is financed well into 2017 and through several important milestones.

Loxo Oncology - Upcoming Milestones

Milestone	Timing
Data from Phase Ia dose-escalation of LOXO-101 in solid tumors	H1:15
Initiate Phase Ib trial on LOXO-101 in patients with TRK-driven tumors	Q2:15
Disclose molecular target of LOXO-200 (undisclosed oncology target)	Mid 2015
Advance companion diagnostic for LOXO-101	2015
File IND for LOXO-200 (undisclosed oncology target)	YE:15
Data from Phase Ib LOXO-101 expansion cohorts	Late 2015/Early 2016

Source: Cowen and Company

Multiple factors support our positive investment recommendation on LOXO shares. These include (1) the company's focus on targeted therapeutics for cancer, an area of medicine we find compelling; (2) an efficient R&D strategy that features the potential for early confirmation of efficacy; (3) a modest valuation (~$208MM market cap, ~92MM enterprise value) that should permit plenty of upside in the event of success; and (4) a credible and experienced management team. On the other hand, these factors should be weighed against that fact that Loxo is an early stage company pursuing mostly a "virtual" business model and that competition in the company's area of focus is likely to be intense.

We chose to value LOXO shares based on a sum-of-the-parts analysis that conservatively assigns value only to LOXO-101's opportunity in lung cancer and the company's net cash position. Should LOXO-101 achieve peak WW sales of $535MM in 2029, our NPV analysis suggests this opportunity could be worth $12-13/share to Loxo assuming the company holds 100% U.S. rights and receives a 25% royalty on ex-U.S. sales. Inclusive of Loxo's net cash position ($7.27/share), our sum-of-the-parts analysis suggests shares may be ~50% undervalued when ascribing no value to LOXO-101's potential in other solid tumors or its pipeline and collaboration with Array Biopharma.

LOXO: Sum-Of-The-Parts Valuation

LOXO-101 NPV In NSCLC	$12.49
Net Cash	$7.27
LOXO-101 NPV In Other Solid Tumors	$0.00
Platform Technology	$0.00
Sum-Of-The-Parts Value	$19.76

Source: Cowen and Company

Loxo Oncology Quarterly P&L ($MM)

	Q1:14A	Q2:14E	Q3:14E	Q4:14E	2014E	Q1:15E	Q2:15E	Q3:15E	Q4:15E	2015E
LOXO-101 Revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Collaborative and Grant Revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Revenue	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
GMs										
R&D	2.0	3.2	4.6	5.5	15.2	5.6	5.8	5.9	6.0	23.3
SG&A	0.9	2.0	2.4	2.6	7.9	2.6	2.7	2.8	2.9	11.0
Total Expenses	**2.9**	**5.2**	**7.0**	**8.1**	**23.1**	**8.2**	**8.5**	**8.7**	**8.9**	**34.3**
Operating Income/Loss	**(2.9)**	**(5.2)**	**(7.0)**	**(8.1)**	**(23.1)**	**(8.2)**	**(8.5)**	**(8.7)**	**(8.9)**	**(34.3)**
Non-Operating Income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Accretion of Redeemable Convertible Stock										
Pre-tax Income/Loss	**(2.9)**	**(5.2)**	**(7.0)**	**(8.1)**	**(23.1)**	**(8.2)**	**(8.5)**	**(8.7)**	**(8.9)**	**(34.3)**
Tax rate (%)	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Provision for income taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	**(2.9)**	**(5.2)**	**(7.0)**	**(8.1)**	**(23.1)**	**(8.2)**	**(8.5)**	**(8.7)**	**(8.9)**	**(34.3)**
GAAP EPS	**($1.06)**	**($1.93)**	**($0.47)**	**($0.50)**	**($2.55)**	**($0.50)**	**($0.51)**	**($0.51)**	**($0.52)**	**($2.05)**
Diluted Shares	2.7	2.7	14.7	16.1	9.1	16.3	16.6	16.9	17.2	16.8

Source: Cowen and Company

Loxo Oncology Annual P&L ($MM)

	2013A	2014E	2015E	2016E	2017E	2018E	2019E
LOXO-101 Revenue	0.0	0.0	0.0	0.0	0.0	0.0	25.0
Collaborative and Grant Revenue	0.0	0.0	0.0	50.0	0.0	50.0	0.0
Total Revenue	**0.0**	**0.0**	**0.0**	**50.0**	**0.0**	**50.0**	**25.0**
COGS	0.0	0.0	0.0	0.0	0.0	0.0	2.5
R&D	9.7	15.2	23.3	34.0	47.0	52.0	55.0
SG&A	0.6	7.9	11.0	12.5	15.0	18.0	60.0
Total Expenses	**10.3**	**23.1**	**34.3**	**46.5**	**62.0**	**70.0**	**117.5**
Operating Income/Loss	(10.3)	(23.1)	(34.3)	3.5	(62.0)	(20.0)	(92.5)
Non-Operating Income	0.0	0.0	0.0	0.0	0.0	0.0	1.0
Pre-tax Income/Loss	(10.3)	(23.1)	(34.3)	3.5	(62.0)	(20.0)	(91.5)
Tax rate (%)	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Provision for income taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Income (Loss)	(10.3)	(23.1)	(34.3)	3.5	(62.0)	(20.0)	(91.5)
GAAP EPS	**($6.64)**	**($2.55)**	**($2.05)**	**$0.15**	**($2.30)**	**($0.65)**	**($2.85)**
Diluted Shares	1.6	9.1	16.8	23.0	27.0	31.0	32.0

Source: Cowen and Company

A Selective Approach To Cancer Drug Discovery

Loxo aims to develop specific and potent targeted therapies for highly selected tumor sub-populations. The Loxo team bases its drug discovery approach on three core competencies (1) appropriate target identification, (2) a leading chemistry platform capable of generating best-in-class small molecules, and (3) the design and execution of a nimble clinical development plan.

1. Target Selection Relies On The Identification Of Oncogenic Drivers

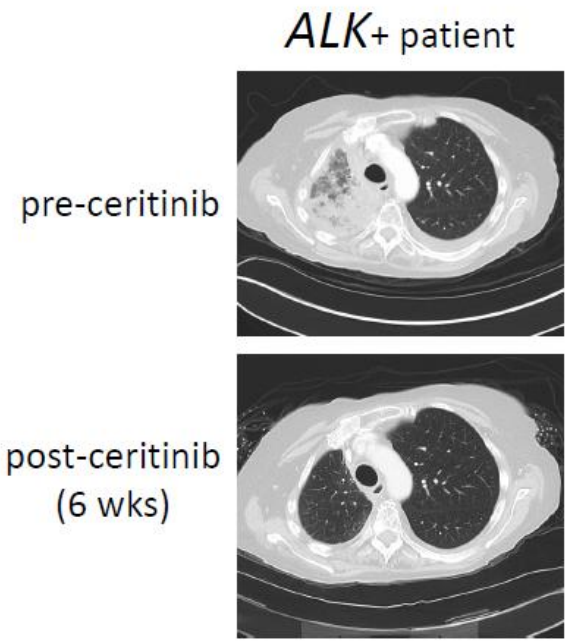
Loxo places great importance on choosing drugable targets that have the potential to exhibit maximal clinical impact. Loxo's management and Scientific Advisory Board use

their extensive oncology expertise to identify targets that are **oncogenic drivers**, or proteins responsible for the initiation and progression of cancer. Genetic alterations (including point mutations, gene amplifications, gene fusions caused by translocations, inversions, deletions) that impart oncogenic properties to a protein are known as **driver alterations**. These are distinct from **passenger mutations**, which are present in cancer cells but do not contribute to their transformation. Cancers that depend for their survival and growth on the activity of oncogenic driver mutations are considered to be addicted. The phenomenon of **oncogene addiction** has attracted considerable attention from the medical and drug development communities. This is because tumors that show dependence on a specific mutation are likely to be highly susceptible to small molecule inhibitors directed against the corresponding oncogene. One area in which this treatment paradigm has been particularly successful is lung cancer. Tumors driven by aberrations in EGFR and ALK have been shown to be highly responsive to small molecule inhibitors directed at these protein kinases. For example, single agent response rates to Tarceva in lung cancer are approximately 65% while drugs like PFE's Xalkori achieve response rates of ~60% in lung cancer patients with ALK alterations.

About half of the targets Loxo is working on have already been clinically validated (less risky, more competition), while the other half are novel (less competition, more development risk). Loxo's strategy to identify the most promising targets from within these categories relies on:

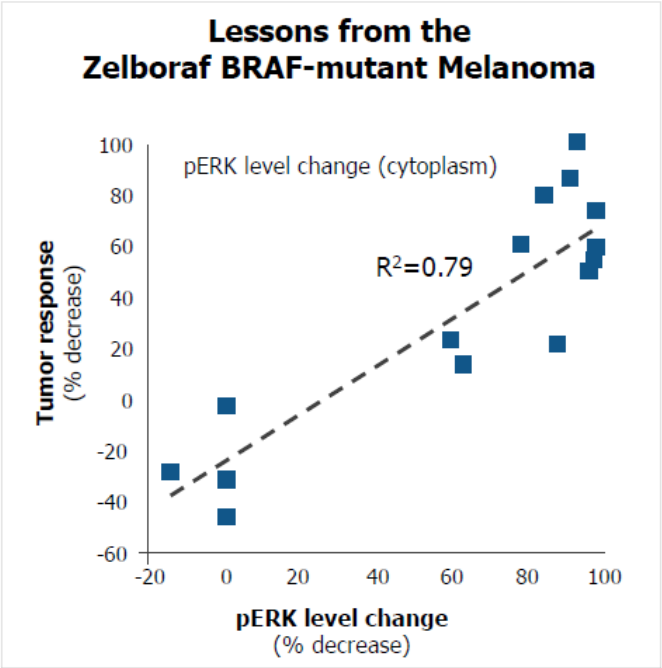
Learning from Clinical Trial Data. Loxo mines clinical trial databases on third-party drugs that have already demonstrated efficacy signals, but have suboptimal PK/PD profiles. Loxo believes that numerous drugs fail not because they are designed against the wrong target, but because they don't fully engage their target. It has been shown that most robust tumor regression occurs when over 80% of the kinase pathway is inhibited (as measure by phosphorylation of downstream targets). This principle is known as **target coverage** and it's been gaining traction in drug development. The company hopes to identify drugs with poor target coverage resulting from subpar pharmacologic properties and redesign the chemistry to overcome these limitations.

Tumor Regression In ALK+ Lung Cancer Patients After Treatment With ALK Inhibitor



Source: Loxo Oncology

Tumor Response Is Correlated With The Extent of Kinase Inhibition Measured By Phosphorylation Of Downstream Targets



Source: Loxo Oncology

Learning from Academic Research. Another approach to target identification is to analyze data emerging from academic labs (publications, conferences, collaborations), or the emerging datasets from studies that seek to analyze the cancer genomes of different tumor types. Novel targets require more extensive experimental work in pre-clinical models to confirm the target is indeed an oncogenic driver, but could also allow Loxo to achieve first mover advantage.

2. Access To Leading Chemistry Via Partnership With Array

Loxo strongly believes that the key to successful drug discovery is good chemistry. In order to discover small molecule inhibitors with optimal pharmacologic properties, Loxo has turned to Array Biopharma. Array's drug discovery capabilities in the area of cancer and inflammatory diseases are recognized as some of the best in the industry. Companies such as Amgen, Celgene and Genentech have engaged Array in their drug development efforts. Array possesses a vast and mature kinase chemistry library, a database of ~4,000 crystal structures, extensive capabilities in high throughput lead identification, protein-structure-enabled drug design, and expertise in diverse chemistry approaches. Of the 16 compounds that Array has advanced into Phase I, 15 of them have met safety and PK goals.

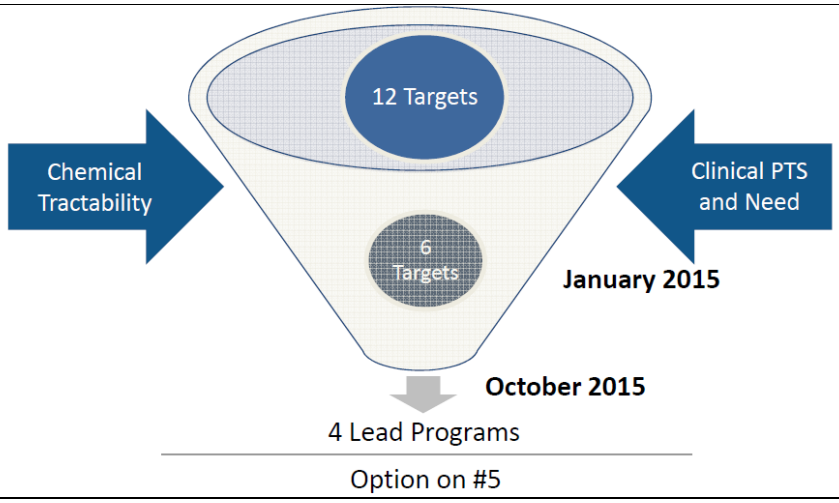
By using the crystal structures of the targeted kinase, as well as related kinases to guide design, Array can deliver small molecules with high affinity and specificity. This is critically important in the world of kinase inhibition for oncology as activity against one of the other ~500 human kinases could be associated with toxicity that prevents a drug candidate from achieving target coverage. In addition, Array is adept at creating small molecules with superior pharmacological properties such as bioavailability and solubility that are critical to *in vivo* activity, Array will provide to Loxo the necessary

support in compound generation and lead optimization as well as pre-clinical testing and Phase 1 drug supply.

Through its collaboration with Array, we believe Loxo has found a cost- and time-effective means to fill its pipeline with viable candidates. In exchange, Array receives monthly FTE support, ~10% equity stake in Loxo, up to $434MM in milestone payments (back end weighted), and mid-single digit royalties on sales of any resulting drugs. For each target addressed under the collaboration, Loxo will owe Array less than $10MM in total development milestones payable at the initiation of Phase II and Phase III trials.

The multi-year and multi-target license and collaboration deal gives Loxo unencumbered worldwide rights to its most advanced clinical candidate (LOXO-101, TRK program) and four other candidates against (undisclosed) targets that are exclusive to Loxo. At any point over the life of the agreement, Loxo is able to swap in any of the four targets, provided that the new target is not being developed as part of Array's internal programs or it is not covered by an agreement with a different Array partner. A fifth candidate target can be acquired for an additional fee. To narrow down to its four exclusive targets, Loxo is exploring the viability of 12 targets. At this point in the process, targets will be prioritized based on their chemical tractability and potential for fast progress through clinical development. By January 2015, the company plans to eliminate six of the candidates with the goal of locking in the four exclusive targets by October 2015.

Loxo Enters Multi-Target Deal With Array Biopharma: Timeline For Target Identification



Source: Loxo Oncology

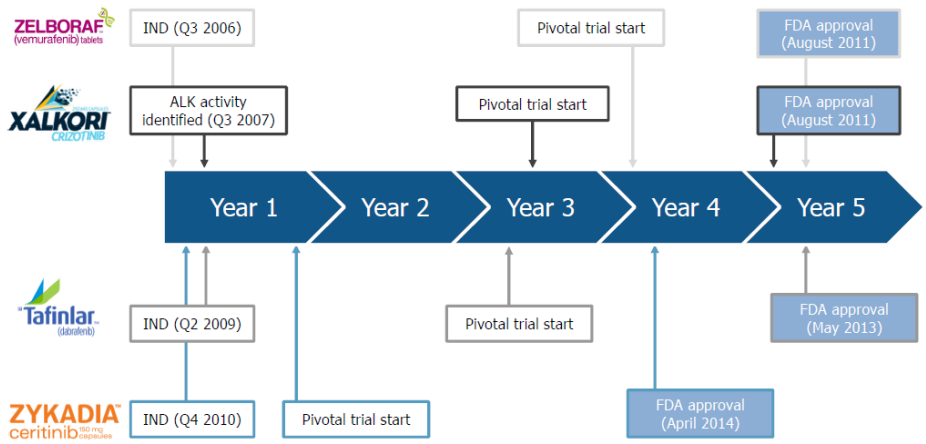
3. Loxo Candidates May Benefit From An Expedited Clinical Program

All the targets pursued by Loxo fall in the category of oncogenic drivers. Such targets have emerged as a privileged category in drug development, yielding success stories like EGFR and ALK inhibitors in lung cancer, BCR-ABL inhibitors in chronic myelogenous leukemia, and BRAF inhibitors in melanoma. What sets these targets apart is that (1) target inhibition observed pre-clinically often translates into a profound clinical response and (2) the objective measures of tumor response tend to be observed early in clinical development, thus de-risking the program. Following an

initial Phase I dose-escalation trial, Loxo's strategy is to immediately enroll patients with driver alterations into its clinical trials.

Another notable feature of Loxo's targets is that they define a relatively narrow subset of cancer patients. Based on the relatively small number of patients targeted as well as the high unmet need in oncology, Loxo may apply for Fast Track Designation from the FDA and seek accelerated approval pathways for registration. Assuming the FDA accepts single-arm trials with response rate endpoints, years could be cut off the standard development timeline. For example, the first FDA approval of an ALK inhibitor (PFE's Xalkori) occurred less than 5 years after the discovery that ALK rearrangements were responsible for driving a subset of lung cancers. Other targeted therapies have witnessed similarly rapid development timelines.

Expedited Clinical Development Programs For Targeted Oncology Drugs



Source: Cowen and Company

Companion Diagnostic Test For TRK Rearrangements

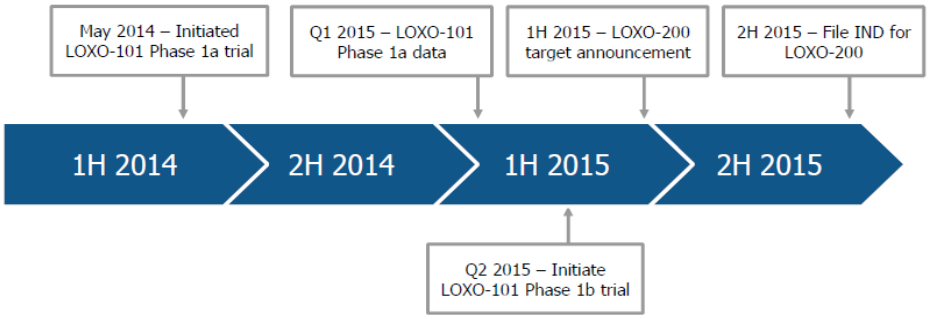
One challenge faced by the developers of targeted drugs for oncology is how to develop a companion diagnostic to identify patients suitable for therapy. Such a diagnostic must be approved by the FDA and EMA concomitantly with the drug candidate.

Screening for specific chromosomal rearrangements is becoming part of the treatment paradigm in many cancers, including lung cancer, and should facilitate Loxo's ability to identify patients with various mutations. For example, Foundation Medicine and Harvard's MGH have already included the ability to detect TRK rearrangements in their assays. In order to further broaden education and awareness of TRK alterations, Loxo is working with an undisclosed technology partner to develop a proprietary companion diagnostic. Loxo has not divulged the specific methodology it intends to use for identifying TRK alterations, but a next-generation sequencing (NGS) platform might be preferred. NGS allows for comprehensive identification of all types of alterations (e.g. fusions, translocations, inversions, amplifications, deletions, or point mutations). Full capture of all alterations via an NGS approach has led investigators to estimate that the frequency of driver ALK mutations in lung cancer might be as high as 8%, up from the 3% that was initially assumed based upon early work on ALK fusions.

Lead Candidate LOXO-101 In Phase I Development

Loxo was quick to recognize the potential of TRK inhibition in cancer and promise of ARRY-470 (now LOXO-101), a highly selective and potent inhibitor of the tyrosine kinase portion of TRK transmembrane receptors (tropomyosin-receptor-kinase). TRK rearrangements have occasionally been uncovered in a variety of cancers in studies dating back 20+ years. However, in most of these instances, TRK's role in driving oncogenesis was not clearly established. Being a relatively infrequent alteration, and in the absence of further molecular characterization, drug developers did not necessarily view TRK as a viable oncology target. However, in 2012 NGS indicated that lung cancer samples negative for other known genetic alterations harbored two novel NTRK1 gene fusions. Full molecular characterization of these gene fusions revealed that they had the potential to act as oncogenic drivers in otherwise healthy cells. Loxo jumped on this finding, and acquired full worldwide rights to LOXO-101 from Array. With the pre-clinical work largely completed by Array, Loxo swiftly advanced the drug candidate into Phase 1a trial in April 2014. Data from this trial should be available in early 2015. Beyond LOXO-101, the company's next clinical candidates against undisclosed targets are at the pre-clinical stage. Target announcement is anticipated in mid-2015, followed by an IND submission late 2015.

Loxo Target Development Timeline



Source: Loxo Oncology

The Biological And Clinical Relevance of Trk Receptors

The Trk family of tyrosine protein kinase receptors is comprised of three distinct but homologous receptors that control important signaling pathways in cells. The TRK receptors, TRKA, B and C, are encoded by three genes (NTRK1, 2, and 3) located on different chromosomes. When the genes are expressed, the protein products fold into transmembrane receptors which are inserted in the plasma membrane with the ligand binding domains facing the extracellular environment and the tyrosine kinase towards the intracellular compartment. While the extracellular domains of the three TRKs share modest sequence homology, the kinase domains are highly conserved (~71% identity). Not surprisingly, molecules targeting the tyrosine kinase domain tend to inhibit all three receptors. In the context of normal TRK function, the kinase domains are activated by binding of the cognate "neurotrophin" ligands to the extracellular immunoglobulin-like domains. TRKA is activated by binding of either NGF (nerve growth factor) or NT-3 (neurotrophin-3), TRKB reacts to binding by BDNF (brain-derived neurotrophic factor) or NT-4 (neurotrophin-4), and TRKC is turned on by an interaction with NT-3 (neurotrophin). Ligand binding induces receptor homodimerization, which brings into close proximity two kinase domains allowing for

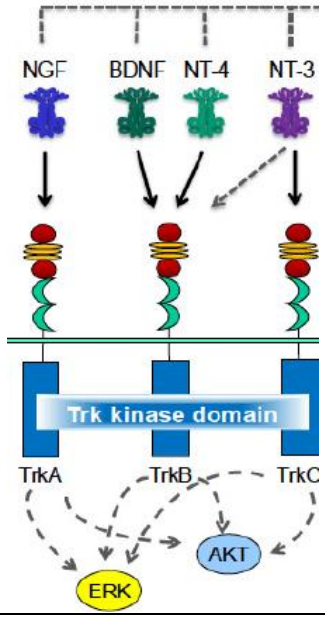
activation and transphopshorylation. As a result of phosphorylation, docking sites are created for a series of effectors that propagate the signal downstream to the Ras/MAPK and AKT pathways. In the case of TRKA, the signaling cascade culminates with the engagement of transcription factors that induce expression of genes implicated in survival and neuronal differentiation.

TRK Family of Receptors, Ligands And Their Function.

Gene	Protein	Cognate Ligand	Function
NTRK1	TRKA	NGF (nerve growth factor); NT-3 (neurotrophin -3)	Pain, Thermoregulation
NTRK2	TRKB	BDNF (brain-derived neurotrophic factor); NT-4 (neurotrophin-4)	Movement, Memory, Mood, Appetite, Body Weight
NTRK3	TRKC	NT-3 (neurotrophin)	Proprioception

Source: Cowen and Company

Signaling Cascades Controlled By TRKs And Cognate Ligands



Source: Loxo Oncology

TRK receptors are thought to play an essential role in the development and maturation of the central and peripheral nervous systems, but not elsewhere in the body. TRKA knockout mice exhibit dramatic losses of peripheral sensory and sympathetic neurons, and die soon after birth. Using a reverse conditional knockout technique, expression of TRKA was restored exclusively to neuronal cells, while expression continued to be absent elsewhere. These mice were viable, and showed no visible phenotype, confirming that lethality is caused by the lack of TRKA function in the nervous system, and that its function is not essential elsewhere in the body. Consistent with these findings, in pre-clinical work with TRK inhibitors that cross the blood-brain barrier, ataxia was observed. Hence Loxo believes that compounds inhibitors of TRK that cross the blood-brain barrier are likely to cause toxicity and should be avoided. Loxo notes that at 60-80X the expected therapeutic concentration of LOXO-101 it sees minimal brain penetration in animal models.

Outside of the brain, TRKs are not expressed at high levels. Inhibiting TRKA signaling elsewhere in the adult body, including the peripheral nervous system, does not seem to pose grave safety concerns. Evidence supporting this claim comes from pain trials in adults suffering from osteoarthritis. In these patients, ablation of NGF-TRKA signaling had a potent effect on pain, while exhibiting a satisfactory safety profile, aside from complications brought about by the underlying disease.

Inhibiting NGF-TRKA Signaling Leads To Effective Pain Control

The involvement of NGF-TRKA signaling in the mediation of chronic pain drew the attention of drug developers. NGF is an inflammatory factor, which is released in response to inflammation in the body. Binding of NGF to TRKA present on nerve cells turns on an ERK-mediated signaling cascade that increases the targeting of transient receptor potential (TRP) channels to the plasma membrane, thus augmenting excitability of pain neurons. These findings led to the development of a number of anti-NGF monoclonal antibodies in an attempt to block this pain pathway. Data from osteoarthritis trials led by Pfizer, Amgen and Regeneron provided evidence that blocking NGF-TRKA signaling is equally if not more efficacious than opioids or NSAID in managing pain. In a Phase II trial for tanezumab (Pfizer's anti-NGF antibody) in knee osteoarthritis, administering the antibody every 8 weeks reduced the pain by a mean of 45-60% from baseline vs. 22% for placebo. Pfizer's drug was to become the first in a new class of drugs for general pain, when in 2010 the FDA halted clinical trials after too many patients in tanezumab's Phase III osteoarthritis trials developed progressively worsening osteoarthritis with evidence of bone necrosis. The only trials allowed to continue were those testing anti-NGF in terminal cancer patients. In November 2012, an FDA Arthritis Advisory Committee agreed that this class of drugs is linked to joint destruction, but unanimously voted for the pain trials to continue as (1) there's a dearth of pain treatments and the benefits outweigh the risks for this drug class (2) the mechanisms by which anti-NGF antibodies lead to joint destruction is not clear. As disease progression and joint destruction was not seen in animal models, it is possible that inhibiting the NGF-TRKA signaling pathway is so anesthetizing that patients overuse their joints. It is unclear, however, why joint overuse would result in necrosis. Based on what has been observed thus far, and as a precaution, the FDA recommended to avoid the use of high doses of anti-NGF and the co-administration of NSAIDs. Pfizer is performing additional pre-clinical toxicology studies which it plans to submit to the FDA in H2:15 in a bid to restart development of tanezumab.

NTRKs As Oncogenic Drivers

Deregulation of TRK receptor activity has been linked to a number of human disorders. Notably, gene alterations giving rise to constitutively active TRKs have been found across multiple tumor types.

TRK Fusions Identified From Cancer Patient Samples Lacking Known Oncogenic Drivers

Gene Fusion	Cancer	1-4%	5-25%	>25%	Unk.
NTRK1	Papillary thyroid cancer		✓		
NTRK1	Spitz neoplasms nevi		✓		
NTRK1	Lung adenocarcinoma	✓			
NTRK1	Lung large cell neuroendocrine cancer	✓			
NTRK1	Intrahepatic cholangiocarcinoma	✓			
NTRK1	Glioblastoma	✓			
NTRK1	Colorectal cancer				✓
NTRK2	Astrocytoma	✓			
NTRK3	Secretory breast carcinoma			✓	
NTRK3	Mammary analogue secretory carcinoma (MASC) of the salivary glands			✓	
NTRK3	Papillary thyroid cancer (post-radiation exposure)		✓		
NTRK3	Congenital mesoblastic nephroma		✓		
NTRK3	Papillary thyroid cancer	✓			
NTRK3	Acute myeloid leukemia	✓			
NTRK1/2/3	Pontine glioma		✓		

Source: Loxo Oncology

In many of these cases, the role, if any, played by TRK in promoting oncogenic transformation has not been established. Frequently, however, the TRK alterations encountered have the hallmarks of oncogenic drivers. Namely, **(1)** the alterations are often fusions, found commonly in patients with solid tumors, **(2)** the fusions contain an intact TRK kinase (signaling) domain, **(3)** the fusion partner provides and activating sequence that might lead to constitutive TRK signaling, and, **(4)** no other known oncogenic drivers are detected in the same samples.

In cancers, much like in its natural state, a fused TRK kinase domain can become activated through a dimerization event. In tumors, however, dimerization is promoted aberrantly and in the absence of external ligand binding. This ligand-independent activation can serve as a driving mechanism for tumorigenesis. Tumors that become dependent for survival and proliferation on TRK kinase activity are considered to be addicted to this oncogene.

To qualify as a *bona fide* oncogenic driver, a TRK fusion must be confirmed experimentally to exhibit one or both the following:

1) Demonstrate that this gene fusion alone is capable of oncogenic transformation when introduced into an otherwise normal cell line or animal;

2) Show that inhibition of the gene product leads to loss of cell proliferation in cells or animals harboring the gene fusion. This is most commonly accomplished via use of RNAi knockdown techniques, small molecule inhibitors, or the transfection of cells with a fusion protein containing a dead version of the kinase.

TRKA Fusions Pass The Test

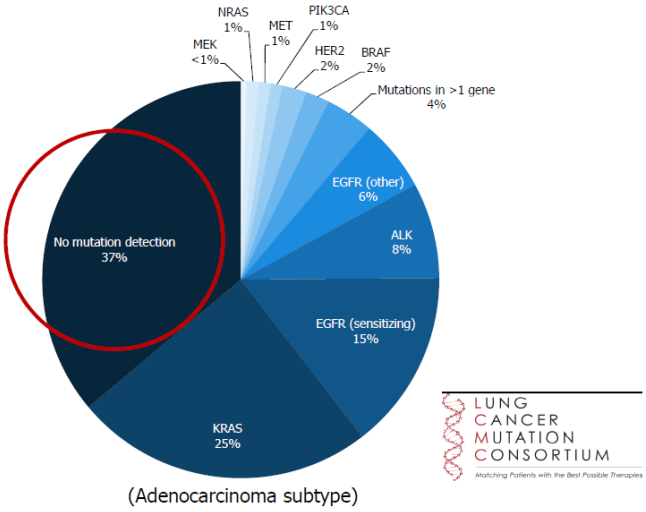
The most comprehensive assessment of TRK fusions as oncogenic drivers was undertaken by Robert Doebele at the University of Colorado. In November 2013, Doebele's lab published a *Nature Medicine* paper (Vaishnavi et al.) identifying TRKA fusions as gene rearrangements with oncogenic potential in lung cancer.

Using next-generation sequencing, Vaishnavi et al. combed the genomes of 36 tumor samples derived from patients with lung adenocarcinoma for which no known mutation could be identified. In two of the patients (females, non-smoker) they detected 2 novel gene fusions involving the kinase domain of NTRK1. In one instance, the NTRK1 gene was fused to the 5' end of the myosin phosphatase-Rho-interacting protein gene (MPRIP), a gene involved in actin skeleton regulation. In the second case, NTRK1 was fused to the major histocompatibility complex (MHC) class II invariant chain (CD74), a known activating fusion of ROS1. To further validate this discovery, the lab created a *break-apart* FISH assay that uses NTRK1 probes of two different colors. The probe that binds to the 5' of NTRK1 is green, while the one that binds to the 3' of the gene is red. When the gene is intact, the green and red dots reside side by side. In the case of gene rearrangements involving NTRK1, the two colored dots are separated (*broken apart*) with the staining pattern dictated by the type of genomic rearrangement. Using this detection method, they were able to confirm the presence of aberrant rearrangements in the cells containing MPRIP-NTRK1 and CD74-NTRK1 gene fusions. Using the same FISH assay, they probed 56 additional lung adenocarcinoma samples selected for lacking of identifiable genetic alterations. In doing so, they found one more sample harboring an NTRK1 rearrangement, but did not analyze it further to identify its fusion partner.

To establish MPRIP-NTRK1 and CD74-NTRK1 as true oncogenic drivers, the lab demonstrated their ability to induce proliferation. By using siRNAs directed at NTRK1 as well as TRKA kinase dead constructs, they were able to show that proliferation is dependent on the TRK kinase activity. Cells expressing the CD74-TRKA fusion construct were injected into nude mice giving rise to tumor growths suggesting that the gene fusion can induce tumorigenesis. Finally, treatment of Ba/F3 cells expressing MPRIP-NTRK1 fusion with increasing concentrations of LOXO-101 resulted in the down regulation of pathways downstream of TRKA, as assessed by phosphorylation levels (western blot). Consistent with this observation, titration of LOXO-101 inhibits proliferation of these cells. Taken together these data strongly suggest that NTRK1 fusions found in lung adenocarcinomas devoid of other known oncogenic alterations, are likely responsible for driving tumorigenesis. As such, they constitute potentially viable drug targets in an indication with tremendous market potential.

At ASCO 2014, a public biotechnology company Ignyta (RXDX, not covered) announced that a TRKA-positive colorectal cancer patient treated with RXDX-101, an oral pan-TRK, ROS1 and ALK inhibitor, achieved a partial response to therapy after only two treatment cycles. This case report further validates a putative oncogenic role for TRKA fusions.

A Substantial Portion Of Lung Cancers Have No Known Driver Mutations



Source: Loxo Oncology

Translocations Involving The Kinase Domain of TRKA Behave As Oncogenic Drivers

Source: Loxo Oncology

Frequency Of TRK Alterations In Lung Cancer

Establishing the incidence of TRK fusions or other TRK driver mutations with any accuracy is not trivial. In the Doebele study, 3 out of 91 preselected lung adenocarcinoma patient samples that did not harbor any known mutations appeared to contain NTRK1 gene fusions. Other studies, however, including a recent *Nature* paper from the Cancer Genome Atlas Research Group (July 2014) analyzing 230 tumor samples, have failed to detect evidence of NTRK1 fusions. Loxo believes this may relate to the use of conservative search algorithms.

If we assume that 37% of lung cancers have no known driver mutations, then a 3.3% incidence within this group suggests that 1.2% of the general lung adenocarcinoma cancer population might have TRKA fusions. A roughly similar incidence, 1.1%, was detected by the same group, this time when analyzing an unselected pool of 447 tumor samples from NSCLC patients. Using the same *break-apart* FISH technique, the authors were able to identify five NTRK1-positive patients (5/443, ~1.1%). Of the five tumors, 3 were adenocarcinoma, 1 squamous cell carcinoma, and 1 large cell neuroendocrine carcinoma. Each of the patients was harboring novel TRKA fusions confirmed by RT-PCR (C18ORF8-NTRK1, RNF213-NTRK1, TBC1D22A-NTRK1, C20ORF112-NTRK1, DNER-NTRK1).

In addition to these gene fusions, the FISH assay revealed 5 additional samples with atypical cytogenic patters and 7 that demonstrated focal NTRK1 gene amplification that will need to be further explored by different methodologies. Should these 12 NTRK1 gene alterations have the ability to drive tumorigenesis, then the incidence of TRKA driver alterations might be as high as 4% (17/443). However, the contribution of gene amplifications to tumorigenesis has been harder to pin down as finding the right threshold of activity necessary for oncogenicity is difficult. Therefore, it is unclear if the additional NTRK amplifications observed by FISH analysis will contribute meaningfully to the frequency of NTRK oncogenic drivers.

LOXO-101: A Potent Pan-TRK Inhibitor With Best In Class Selectivity

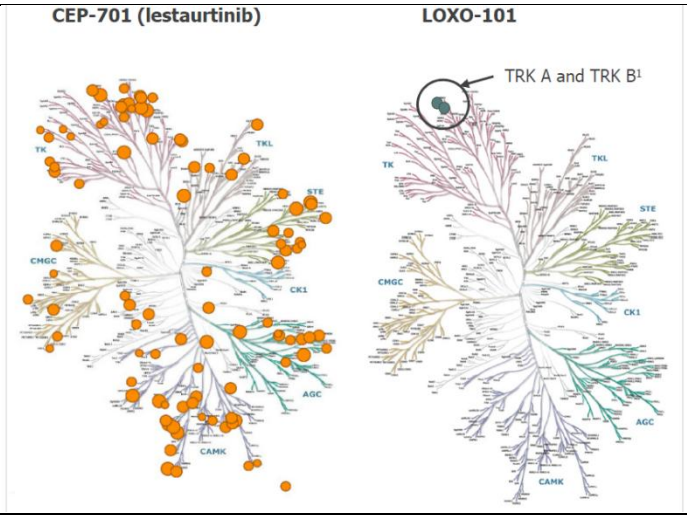
Clinical experience has shown that "addiction" makes tumors particularly vulnerable to drugs that disrupt the activity of an oncogene. It is therefore expected that a TRK inhibitor could be highly potent in tumors driven by this oncogene. Loxo holds worldwide rights to a potent and selective oral pan-TRK inhibitor (LOXO-101) that in pre-clinical work has demonstrated best-in-class pharmacological properties. Inspired by the clinical potency of neutralizing anti-NGF antibodies in chronic pain trials, Array originally designed LOXO-101 to suppress the NGF-TRKA signaling pathway by silencing the kinase domain of TRKA. Therefore, LOXO-101 was developed to meet the high safety requirements for pain treatment, including maximum selectivity for the TRK receptors. The drug was designed **not** to penetrate the blood-brain barrier. Given the importance of TRK receptors to the development of the nervous system, TRK inhibitors that penetrate into the brain might cause neurocognitive defects. Ataxia has been seen in animal models treated with TRK inhibitors that do cross the blood-brain barrier. The company noted that LOXO-101 toxicology data were unremarkable. Toxicology studies in rats and monkeys demonstrated reversible increases in liver enzymes.

LOXO-101 Has Excellent Pharmacologic Drug Properties

PROPERTY	DESCRIPTION
Selectivity	TRK A, B, C Limited inhibition of other kinases
Potency	Low nM potency against TRK A, B, C (cell & enzymatic)
Oral Bioavailability	High, in 4 preclinical species Initial human PK data from 1st cohort of Phase 1 demonstrate good exposure
Protein Binding	Moderate
Safety	No relevant hERG inhibition No preclinical QT findings
Dosing	Phase 1: oral, continuous 28 day cycle
Toxicity	Wide safety margin at expected therapeutic doses. Animals show no body weight loss and no drug-related deaths at high doses.

Source: Loxo Oncology

LOXO-101 Is A Highly Specific Inhibitor of TRK Receptors



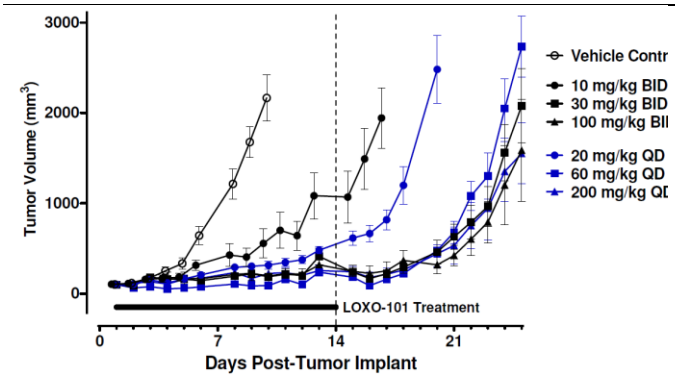
Source: Loxo Oncology

A striking property of LOXO-101 is its high selectivity. The drug has demonstrated limited inhibition of other kinases (see dendrogram above). LOXO-101 has 38-fold selectivity for TRK receptors over the next closest kinase, and 100-fold selectivity over all other kinases. Consistent with this, animal models were virtually free of off target effects. Another trait of high quality kinase inhibitors is low nM potency, which LOXO-101 has against all three TRK receptors, demonstrated both in cell and enzymatic assays. In animal studies LOXO-101 showed good oral bioavailability and moderate protein binding. Binding to proteins restricts the amount of drug available to bind its intended target, which can lower efficacy. About 30% of LOXO-101 is unbound, free drug.

In preparation for clinical trials, the company used pre-clinical data on the pharmacology of LOXO-101, to model PK behavior of the drug in human subjects. To ensure a robust clinical response, the company plans to achieve plasma drug levels

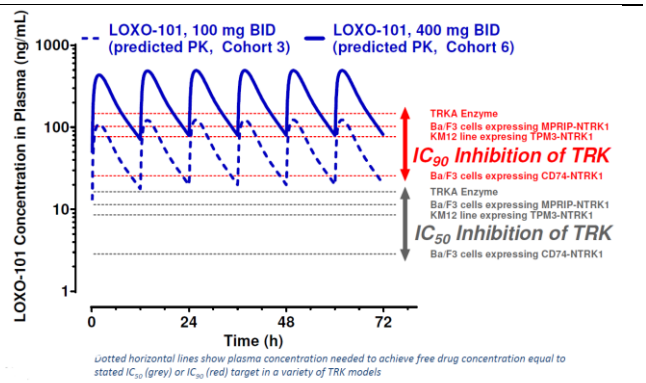
above the IC90. This should be possible given the favorable PK and toxicology data. Loxo's models predict that IC50 inhibition of TRKA in humans would require LOXO-101 concentration in the plasma above 10 ng/mL, while IC90 inhibition can be achieved at plasma concentrations above 100 ng/mL. According to this model, administering LOXO-101 at 100 mg BID, which is the dose given to Cohort 3 in the Phase Ia dose escalation study, should nearly achieve the plasma concentration target for IC90 inhibition. Administering LOXO-101 at 400 mg BID, which is the dose for Cohort 6, should comfortably reach the IC90 target.

Demonstrated Anti-Tumor Activity In a TRKA-Driven Mouse Model of Cancer



Source: Loxo Oncology

PK Modeling In Humans: Predicted Target Coverage Based On Simulation



Source: Loxo Oncology

LOXO-101 is in a Phase Ia dose-escalation trial in patients with solid tumors with data readouts expected in H1:15 and Phase Ib expansion stage anticipated to being in Q2:15. Loxo management has guided that, depending on the response rates observed in the Phase I trials, a single-arm, Phase II trial could be sufficient to support NDA submission. Loxo is planning to develop LOXO-101 for the treatment of tumors with TRK alterations, with initial development focused on TRK+ NSCLC cancer.

Phase I Trial Of LOXO-101 In Solid Tumors

- *Trial initiated: April 2014*
- *Completion of dose-escalation stage: Early 2015*
- *Initial data from dose-escalation stage: H1:15*
- *Initiation of expansion stage: Q2:15*
- *Data from expansion stage: 2015-2016*

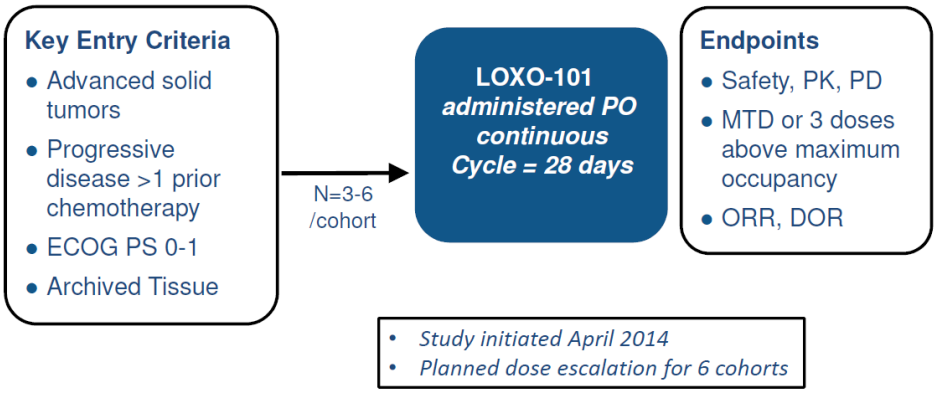
In April 2014, Loxo initiated an open label, multicenter, Phase I trial of LOXO-101 in advanced solid tumors. This trial has two stages: a Phase Ia dose escalation stage and a Phase Ib expansion stage.

Stage 1: In the Phase Ia dose escalation stage, approximately 3-6 patients will be treated in each of six cohorts. The trial is expected to enroll refractory locally advanced or metastatic solid tumor patients. Enrollment in this stage is not restricted to TRK mutated patients. However, patients are only being recruited in centers with genotyping capabilities, hence it is possible that patients identified with TRK

alterations could be preferentially directed into this study. In the Phase Ia stage, patients will receive continuous oral doses of LOXO-101 on a 28-day cycle.

The primary endpoints of the dose-escalation stage are to evaluate the safety, tolerability, PK and PD profile of LOXO-101, including determining the MTD and the optimal dose of LOXO-101. Secondary endpoints include PFS, ORR, and DOR.

Phase Ia Dose Escalation Stage Trial Design



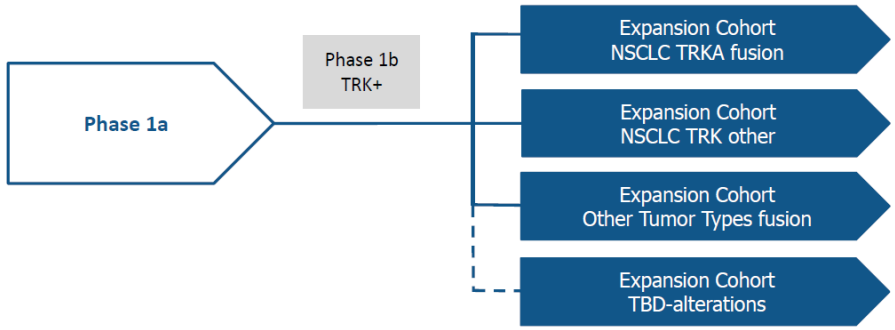
Source: Loxo Oncology

LOXO has completed dosing in the first cohort and enrollment is ongoing in the second dose-escalation cohort. Management noted that bioavailability of LOXO-101 has been in line with the pre-clinical experience, and initial PK data from the first cohort suggest that drug was absorbed with good exposure. In addition, no DTLs were observed in the first cohort. The third cohort will evaluate the BID (twice a day) dosing. LOXO expects to complete the dose-escalation stage by early 2015. Management has guided that data from the Phase Ia cohorts will only be made available at a medical meeting, however, management may be willing to provide enrollment updates during investor meetings/conference calls.

Stage 2: In the Phase Ib expansion stage, Loxo is planning to test one or more dose levels of LOXO-101 in four expansion cohorts. Each expansion cohort will enroll approximately 33 patients carrying TRK alterations. The first cohort is expected to enroll NSCLC TRKA fusion patients; the second cohort is expected to enroll NSCLC patients who have TRKB mutation. The third cohort is expected to enroll TRK+ patients with other tumor types. Management has hinted that this cohort could include patients with papillary thyroid cancer and colorectal cancer. Details of the fourth expansion cohort are yet to be disclosed.

The primary endpoints of the trial are ORR, DOR, PFS, with safety and tolerability as secondary endpoints.

Phase Ib Expansion Stage Trial Design



Objectives	Establish anti-tumor activity; ORR, DOR, PFS
Population	Relapse, no SOC → local TRK testing → central confirmation

Source: Loxo Oncology

What's Next For LOXO-101

Loxo management has guided that, depending on the response rates observed in the Phase Ib trial, a single-arm, Phase II trial could be sufficient to support NDA submission. In lung cancer, an ORR in the 30%+ and a PFS of 6+ months should be sufficient to gain approval.

In order to effectively identify patients whose tumors harbor the relevant genetic alterations, the company plans to collaborate with a partner with diagnostics expertise to develop and commercialize a companion diagnostic for LOXO-101. The management has guided that it is currently exploring options and will have the diagnostic ready before the initiation of pivotal trial(s).

LOXO-101's Commercial Opportunity

We believe LOXO-101 has the potential to be a $200-$300MM+ drug in lung cancer in U.S., and that proven utility outside this indication could substantially broaden its reach. However, as data are lacking to assess the frequency of TRK driver alterations outside of lung cancer, we have limited means to assess the size of any such opportunity. Hence we include only lung cancer in our formal revenue and valuation models for LOXO-101.

Eligible TRK+ NSCLC patient population

According to the National Cancer Institute, approximately 160,000 patients die from lung cancer annually making it the number one cause of cancer deaths in the U.S. There are approximately 224,000 lung cancer patients diagnosed in the U.S. each year. Of these roughly 190,000 (85%) are classified as non-small cell lung cancer (NSCLC). There are two main subtypes of NSCLC: (1) squamous cell carcinoma, 25-30% of all lung cancer cases, (2) non-squamous cell carcinoma, 70-75% of all lung cancer cases. We assume that TRK alterations will be found only in non-squamous cell NSCLC, which represents approximately ~143,000 of all lung cancer cases. Further ~80% of new patients, or 114,000 non-squamous patients are classified as having locally advanced or metastatic disease (Stage III/IV). LOXO-101 is being developed for a specific genetic mutation known as TRK, which according to the literature sources discussed above might be present in 1-4% of non-squamous cell NSCLC patients. In our model, we have assumed the middle of the range, or 2%, this would correspond to 1,700 TRK+ NSCLC patients in the U.S.

LOXO-101 Commercial Rights ex-U.S.

Loxo Oncology owns worldwide rights to LOXO-101 and would likely market the drug on its own in the U.S. For modeling purposes, we have assumed that the company is likely to partner ex-US rights with a larger biopharma, and might receive a 25% royalty on ex-US sales. We have assumed that Loxo will receive a $50MM in upfront payment and another $300M in development, regulatory, and commercial milestones.

Pricing, Peak Penetration and Revenues in TRK+ NSCLC

We assume that, if approved, LOXO-101 is likely to be used in majority of TRK+ NSCLC patients, reaching peak penetrations of 70-75%. The only other inhibitor in clinical development for the treatment of TRK+ NSCLC is Ignyta's RXDX-101. This compound has shown early signs of activity in TRK+ patients. However, for modeling purposes, we assume its development will not interfere with LOXO-101's commercial opportunity, either because the two agents will be used in sequence or because LOXO-101's superior specificity will engender it with a better clinical profile (see the competition section below). Assuming an average treatment cost of $125,000/patient, we project peak U.S. sales of $285MM within the NSCLC market. We model peak ex-U.S. sales of $250MM generating peak ex-U.S. royalties of $62.5MM to Loxo.

LOXO-101 Global NSCLC Revenue Model ($MM)

U.S.	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029
# of cases with NSCLC (000)	190	192	194	196	198	200	202	204	206	208	210
% cases with non-squamous cell carcinomas	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*
# cases with non-squamous cell carcinomas	143	144	146	147	149	150	152	153	155	156	158
% of Stage IIIb/IV disease	*80%*	*80%*	*80%*	*80%*	*80%*	*80%*	*80%*	*80%*	*80%*	*80%*	*80%*
# of Stage IIIb/IV disease	114	115	117	118	119	120	121	122	124	125	126
% of pts eligible for chemotherapy	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*	*75%*
# of pts eligible for chemotherapy	86	87	87	88	89	90	91	92	93	94	95
% of NSCLC patients with TRK alterations	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*
# of NSCLC patients with TRK alterations	1.7	2	2	2	2	2	2	2	2	2	2
LOXO-101 Mkt Share	*12%*	*31%*	*52%*	*65%*	*70%*	*73%*	*74%*	*74%*	*74%*	*74%*	*74%*
# of patients on LOXO-101	0.2	0.5	0.9	1.1	1.3	1.3	1.3	1.4	1.4	1.4	1.4
Price per patient ($000)	$125	$131	$138	$145	$152	$160	$168	$176	$185	$194	$204
U.S. LOXO-101 Revenue ($MM)	**$25.0**	**$70.0**	**$125.0**	**$165.0**	**$190.0**	**$210.0**	**$225.0**	**$240.0**	**$255.0**	**$270.0**	**$285.0**
% growth Y/Y		*180%*	*79%*	*32%*	*15%*	*11%*	*7%*	*7%*	*6%*	*6%*	*6%*
R.O.W.											
R.O.W. LOXO-101 Sales ($MM)	**$0.0**	**$20.0**	**$65.0**	**$100.0**	**$140.0**	**$170.0**	**$190.0**	**$210.0**	**$230.0**	**$240.0**	**$250.0**
As a % of U.S. Sales	*0%*	*29%*	*52%*	*61%*	*74%*	*81%*	*84%*	*88%*	*90%*	*89%*	*88%*
Total WW LOXO-101 Sales ($MM)	**$25.0**	**$90.0**	**$190.0**	**$265.0**	**$330.0**	**$380.0**	**$415.0**	**$450.0**	**$485.0**	**$510.0**	**$535.0**
Loxo Royalty	***25%***	***25%***	***25%***	***25%***	***25%***	***25%***	***25%***	***25%***	***25%***	***25%***	***25%***
R.O.W. LOXO-101 Revenue ($MM)	**$0.0**	**$5.0**	**$16.3**	**$25.0**	**$35.0**	**$42.5**	**$47.5**	**$52.5**	**$57.5**	**$60.0**	**$62.5**
Total WW LOXO-101 Revenue ($MM)	**$25.0**	**$75.0**	**$141.3**	**$190.0**	**$225.0**	**$252.5**	**$272.5**	**$292.5**	**$312.5**	**$330.0**	**$347.5**
% growth Y/Y		*200%*	*88%*	*35%*	*18%*	*12%*	*8%*	*7%*	*7%*	*6%*	*5%*

Source: Cowen and Company

LOXO Might Be Worth $12-13/share on An NPV Basis

Based upon peak WW revenues of just over $500MM in TRK+NSCLC, our NPV analysis suggests this opportunity alone be worth $12-13/share, inclusive of a 15% discount rate to account for its risk profile. Additional upside could be supported by LOXO-101 revenues in other tumor types, or success associated with any of LOXO's other potential pre-clinical candidates.

LOXO-101 NPV Analysis ($MM)

Financial Year End	12/31/2014
Valuation Date	8/29/2014
Discount Rate	**15.0%**
Perpetual Growth Rate	**0.0%**

LOXO Therapeutics NPV

Valuation Date: Friday, August 29, 2014

$MM	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029
LOXO-101 NSCLC U.S. Sales						25	70	125	165	190	210	225	240	255	270	285
Growth (%)								*79%*	*32%*	*15%*	*11%*	*7%*	*7%*	*6%*	*6%*	*6%*
Collaboration Milestones			$50		$50		50.0		50.0		75.0		75.0			
Total Revenue	**0**	**0**	**50**	**0**	**50**	**25**	**120**	**125**	**215**	**190**	**285**	**225**	**315**	**255**	**270**	**285**
									72%	*-12%*	*50%*	*-21%*	*40%*	*-19%*	*6%*	*6%*
COGS	**0**	**0**	**0**	**0**	**0**	**3**	**7**	**13**	**17**	**19**	**21**	**23**	**24**	**26**	**27**	**29**
COGS as a % of total sales						*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*
R&D	**15**	**23**	**34**	**47**	**52**	**55**	**35**	**19**	**3**	**4**	**4**	**5**	**5**	**5**	**5**	**6**
R&D as a % of Revenues							*50%*	*15%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*
SG&A	**8**	**11**	**13**	**15**	**18**	**60**	**63**	**78**	**50**	**42**	**42**	**43**	**43**	**43**	**46**	**48**
SG&A as a % of Revenues							*90%*	*62%*	*30%*	*22%*	*20%*	*19%*	*18%*	*17%*	*17%*	*17%*
Operating Income	**(23)**	**(34)**	**4**	**(62)**	**(20)**	**(93)**	**15**	**16**	**146**	**125**	**218**	**155**	**243**	**181**	**192**	**202**
Operating Margin									*68%*	*66%*	*76%*	*69%*	*77%*	*71%*	*71%*	*71%*
LOXO-101 Royalties						**0**	**5**	**16**	**25**	**35**	**43**	**48**	**53**	**58**	**60**	**12**
Tax	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2**	**9**	**8**	**13**	**41**	**103**	**83**	**88**	**75**
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*5%*	*5%*	*5%*	*20%*	*35%*	*35%*	*35%*	*35%*
Approx Free Cash Flow	**(23)**	**(34)**	**4**	**(62)**	**(20)**	**(93)**	**15**	**15**	**137**	**117**	**205**	**115**	**140**	**98**	**104**	**127**
Years	0.34	1.34	2.34	3.34	4.34	5.34	6.34	7.34	8.34	9.34	10.34	11.34	12.34	13.34	14.34	15.34
Discount Factor	0.95	0.83	0.72	0.63	0.55	0.47	0.41	0.36	0.31	0.27	0.24	0.20	0.18	0.15	0.13	0.12
NPV of Cash flows	**(22)**	**(28)**	**3**	**(39)**	**(11)**	**(44)**	**6**	**5**	**43**	**32**	**48**	**24**	**25**	**15**	**14**	**15**

Terminal Value Calculation

Final year FCF	127
Perpetual Growth Rate	0.0%
Terminal Value	**849**
Discount Factor	0.12
Present Value of Terminal Value	**99**
Present Value of Cash Flows	**102**
Enterprise Value	**201**
Market Value	**201**
Fully Diluted Shares Outstanding	16.1
Value per Fully Diluted Share	**$12.49**

Source: Cowen and Company.

Competition: Selectivity Looks To Be LOXO-101's Strong Suit

There are no approved drugs that target TRK activation. However, there are a number of multi-kinase inhibitors with published activity against TRK. These include Novartis AG's dovitinib, PLX-7486 from Daiichi Sankyo and its subsidiary Plexxikon, Tesaro's TSR-011, and Ignyta's RXDX-101. Relative to these compounds, LOXO-101 appears far more specific for TRK inhibition. As a result, Loxo believes that its competitors may face challenges in achieving full target coverage at dosing levels that are devoid of off-target effects on other kinases (and their associated adverse clinical effects). Loxo also believes that LOXO-101 is differentiated by virtue of superior pharmaceutical properties, including lack of brain penetration. It is unclear whether Novartis and Diachii Sankyo are pursuing their compounds in TRK+ focused subpopulations. However, Ignyta's RXDX-101 is being studied in a Phase I/II trial initiated in July and Tesaro's TSR-011 is enrolling TRK+ patients in one of its Phase I/II cohorts. We discuss these two candidates in more detail below.

TRK Competitors In Clinical Development

Agent	Company	Inhibitor Profile	TRK Development
Dovitinib	Novartis	Flt3, c-Kit, FGFR1-3, VEGFR1-3, PDGFR	Phase 2 in any activated pathway, including TRK
PLX7486	Daiichi Sankyo	Flt3, cFMS	Phase 1 gem, abraxane combo in pancreatic
TSR-011	Tesaro	ALK 10X less for TRK	Phase 1/2a, TRKA cohort included
RXDX-101	Ignyta	Pan TRK, ROS1, ALK	European Phase 1 US IND 1Q14

Source: Loxo Oncology

Ignyta's RXDX-101 Establishes Proof Of Concept For TRK Inhibition

Loxo's main competitor in TRK inhibition might be RXDX-101. RXDX-101 is a potent, oral, ATP-competitive inhibitor of at least five kinases implicated in oncology: TRKA, TRKB, TRKC, ROS1, and ALK. *In vitro*, RXDX-101 was shown to inhibit TRKA, TRKB, TRKC, ROS1, and ALK kinase activity with an IC50 of less than 2nM. The drug, however, is likely to inhibit additional kinases, as suggested by preliminary data from Loxo using a compound synthesized based on the published structure of RXDX-101.

Kinase Inhibition Selectivity Of RXDX-101

Target	TrkA	TrkB	TrkC	ROS1	ALK
IC50 (nM)	1.7	0.1	0.1	0.2	1.6

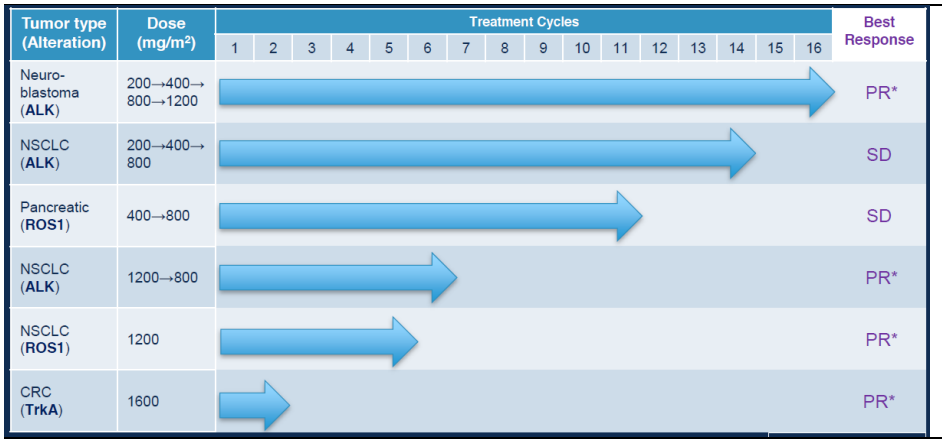
Source: Ignyta's ASCO 2014 presentation

In addition, pre-clinical models have shown that RXDX-101 is capable of crossing the blood-brain barrier. While Ignyta views this as a potentially favorable property that could enable RXDX to target CNS lesions, TRK biology suggests that CNS inhibition is undesired in terms of its potential to cause on-target toxicity. Loxo's studies testing a variety of TRK-inhibitors in pre-clinical models indicated that those that crossed the blood-brain barrier consistently caused ataxia (a loss in voluntary muscle control). Moreover, in a phase I study, PHA-848125, a CDK/TRKA inhibitor with the ability to cross the blood-brain barrier, showed dose-limiting toxicities manifested as ataxia and tremors. Consequently, the drug schedule of patients in this trial had to be switched from daily to 4 days on and 3 days off. Following this study, the development of PHA-848125 stagnated. PHA-848125 was developed by Nerviano, the same company that licensed rights to RXDX-101 to Ignyta.

Interim data from a Phase I trial of RXDX-101 in solid tumors were presented at the 2014 ASCO meeting. This Phase I dose-escalation trial of RXDX-101 in patients with advanced solid tumors with alterations to TRKA, ROS1, or ALK enrolled 20 patients who received escalating oral doses of RXDX-101 in six cohorts (100, 200, 400, 800, 1200, and 1600 mg/m2). Patients received QD doses of RXDX-101 for 4 days a week for 3 consecutive weeks, followed by 1 week off, on a 28-day cycle. The trial is being conducted in Italy. The primary endpoint of the trial was to establish the maximum tolerated dose (MTD) and recommended Phase II dose. As of May 2014, 19 patients (11 ALK+, 7 ROS1+, and 1 TRKA+) had been dosed in the six dose cohorts.

RXDX-101 was shown to have evidence of activity. Clinical responses were observed in 6 patients (4 PRs and 2 SD), and all six remained on active treatment, with three patients having received 12 to 16 cycles. Of interest to Loxo investors is the observation that the TRKA-positive colon cancer patient showed a partial response after only 2 cycles of treatment. This represents the first known TRK-positive patient to respond to a TRK inhibitor establishing some proof of concept for targeting this oncogene.

Phase I trial of RXDX-101: Clinical Responses



Source: Ignyta's ASCO 2014 Presentation

No drug-related SAEs were reported and there were no discontinuations due to AEs. However, treatment with RXDX-101 was associated with significant adverse events. A total of 9 Grade 3 or higher adverse events were observed in patients. There was 1 Grade 5 AE related to respiratory failure, and two Grade 3/4 AEs that were possibly drug-related: a Grade 4 lipase increase and a Grade 3 asthenia. Nausea, paresthesia, asthenia, and vomiting was observed in ~50% of the patients.

RXDX Moving Forward In Phase I/II Trial. In June 2014, Ignyta initiated a global, single-arm, open-label, Phase I/II trial of RXDX-101 in patients with advanced solid tumors with alterations to TRKA, ROS1, or ALK. The trial has two phases and is expected to enroll ~124 patients who will receive continuous daily dosing of oral RXDX-101. Recall that in the above discussed Phase I trial, patients receive intermittent dosing (4 days a week for 3 consecutive weeks, followed by 1 week off, on a 28-day cycle). The primary endpoint of the Phase I portion is to establish the maximum tolerated dose (MTD) and recommended Phase II dose, while the primary endpoint of the Phase II portion is efficacy and safety.

Tesaro Is Also Developing An ALK/TRK Inhibitor

TSR-011 is a dual ALK/TRK inhibitor displaying low nanomolar potency towards these kinases both *in vitro* and in cells. The development of TSR-011 has focused on its ability to inhibit ALK. The drug candidate has been shown to suppress ALK-dependent tumor growth in mouse models, and in a Phase I, dose-escalation and cohort expansion study evaluating safety, tolerability, dosing (DLT and MTD) and pharmacokinetics, it demonstrated some anti-tumor activity in ALK+ lung cancer patients resistant to crizotinib.

Given that TSR-011 also inhibits TRKA with a cellular IC50 of 1.8nM and it is capable of inhibiting cancer proliferation *in vitro* in cells with TRKA gene fusions, Tesaro plans to enroll TRK-positive patients (as defined by immunohistochemistry or FISH) in future trials. The company is planning a Phase IIa study that includes a cohort of TRK+ patients.

At ASCO 2014, Tesaro provided an update on its Phase I dose escalation study. Twenty-three patients suffering from various advanced cancers were enrolled in the trial at daily doses between 30 and 480 mg. Three out of five crizotinib-resistant ALK+ NSCLC patients achieved a partial response. Stable disease was

observed in patients with papillary thyroid, pancreatic and colorectal cancers. Dose limiting toxicities included dysaesthesia and QTc prolongation. The company is attempting to tackle the QTc prolongation issues (likely is related to inhibition of the hERG channel) by altering the PK profile of the drug. The safety prolife of TSR-011 may be further complicated by its inhibition of additional targets, as hinted to by preliminary *in vitro* results obtained by Loxo with a drug synthesized based on the publically available structure of TSR-011.

TSR-011 Is A Potent Inhibitor Of ALK and TRKs In Vitro And Cell Assays

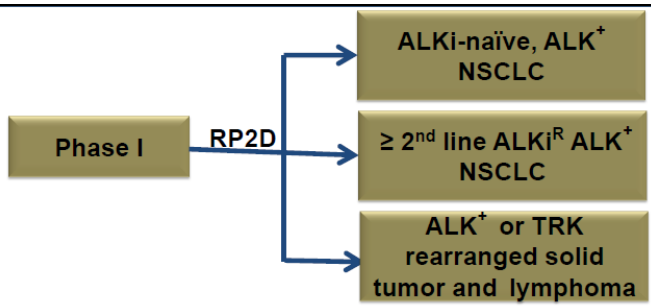
Kinase	Recombinant Protein		Cellular[a] IC50 (nM)
	Kd (nM)	IC50 (nM)	
ALK	0.36	0.7	< 1.0
TRKA	4.7	0.5	1.8
TRKB	1.2	1.5	14.2
TRKC	7.1	2.4	26.9

[a.] Direct comparison of cellular activity was evaluated in engineered BaF3 cell line dependent on the specific kinase for proliferation

Inhibition of Proliferation (IC50: nM)			
H3122 cells *EML4-ALK*	NB-1 cells *ALK amplification*	KM12 cells *TPM3-TRKA*	TF-1 cells *NGF stimulated*
1	10	25	42

Source: Tesaro's ESMO 2013 Presentation

Design For TSR-011 Phase IIa Trial



Source: Tesaro's ESMO 2013 Presentation

A Team Of Experts Guides Loxo To Its Targets

Loxo's scientific and clinical strategy was envisioned by the company's CEO, Dr. Joshua H. Bilenker and the Chair of its Scientific Advisory Board, Dr. Keith Flaherty. Drs. Bilenker and Flaherty trained together at The Johns Hopkins School of Medicine and at the University of Pennsylvania. Between 2004 and 2006, Dr. Bilenker worked in the FDA's Office of Oncology where he served as a Medical Officer. Before becoming CEO of Loxo, Dr. Bilenker was a partner at Aisling Capital, a multi-strategy healthcare investment firm. It was through his duties at Aisling that he became acquainted with Array's specific TRK inhibitor. Together with Dr. Flaherty who is now the Director of Developmental Therapeutics, at the Massachusetts General Hospital Cancer Center, Dr. Bilenker put together the business plan for Loxo and started attracting an impressive team of advisors and employees. Lori A. Kunkel, M.D. is serving as Loxo's Chief Medical Officer. Dr. Kunkel previously served in the CMO roles at Pharmacyclics and Proteolix, where she played a leading role in the development of two recently approved drugs, Imbruvica (ibrutinib) and Carfilzomib (Kyprolis). As Chief Scientific Officer, Mikel P. Moyer, Ph.D. brings to Loxo years of experience acquired while leading the medicinal chemistry teams at Pfizer that discovered Tarceva (erlotinib) and Xelijanz (tofacitinib). Loxo also benefits from EVP Jennifer Low's experience in drug development acquired while at Genentech. An M.D., Ph.D. by training, Dr. Low led the development of Erivedge (vismodegib) as well as supervised the development teams for numerous drug candidates including Zelboraf (vemurafenib), Tarceva (erlotinib) and Cometriq (cobimetinib). Loxo's CFO, Dov Goldstein, joined in July 2014 from his role as a partner at Aisling Capital. Dov has served on a number of biotech company Boards and is the former CFO of Vicuron Pharmaceuticals (acquired by Pfizer).

Loxo's SAB is integral to the company's target discovery and selection process. In addition to Dr. Flaherty, it includes Jeffrey A. Engelman, M.D., Ph.D., Director of The

Center For Thoracic Cancer at Mass. Gen. Hospital Cancer Center; Dr. Ross L. Levine, Chair in Leukemia Research at MSKCC; Ben Ho Park, M.D., Ph.D., Associate Professor of Oncology at John Hopkins University; and Dr. David Solit, Director of the Center For Molecular Oncology at MSKCC.

Loxo Oncology's Scientific Advisory Board

Keith Flaherty, MD	MGH	CLOVIS ONCOLOGY Board of Directors
Jeffrey A. Engelman, MD, PhD	MGH	agios Scientific Advisor
Ross L. Levine, MD	MSKCC	FOUNDATION MEDICINE Research Affiliation
Ben Ho Park, MD, PhD	JHU	The Breast Cancer Research Foundation Research Affiliation
David Solit, MD	MSKCC	Pfizer Research Affiliation

Source: Loxo Oncology

Valuation Methodology And Risks

Valuation Methodology

Biotechnology:

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

Risks To The Price Target

Loxo Oncology is unprofitable, has no approved products, and will likely need to raise additional capital from the public markets prior to turning profitable. Loxo's lead candidate LOXO-101 faces a number of clinical, regulatory, and commercial hurdles prior to becoming successful.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon a an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe it there are any good methodologies for assigning a specific target price to such stocks.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
BLUE	bluebird bio
LOXO	Loxo Oncology
RLYP	Relypsa
SNSS	Sunesis Pharmaceuticals

Analyst Certification

Each author of this research report hereby certifies that (i) the views expressed in the research report accurately reflect his or her personal views about any and all of the subject securities or issuers, and (ii) no part of his or her compensation was, is, or will be related, directly or indirectly, to the specific recommendations or views expressed in this report.

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Loxo Oncology, bluebird bio, Relypsa and Sunesis Pharmaceuticals have been client(s) of Cowen and Company, LLC in the past 12 months.

Cowen and Company, LLC and/or its affiliates expect to receive, or intend to seek, compensation for investment banking services in the next 3 months from Loxo Oncology, bluebird bio and Sunesis Pharmaceuticals.

Loxo Oncology, bluebird bio, Relypsa and Sunesis Pharmaceuticals is or was in the past 12 months a client of Cowen and Company, LLC; during the past 12 months, Cowen and Company, LLC provided IB services.

Cowen and Company, LLC and/or its affiliates received in the past 12 months compensation for investment banking services from Loxo Oncology, bluebird bio, Relypsa and Sunesis Pharmaceuticals.

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COWEN AND COMPANY RATING DEFINITIONS

Cowen and Company Rating System effective May 25, 2013

Outperform (1): The stock is expected to achieve a total positive return of at least 15% over the next 12 months

Market Perform (2): The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform over the next 12 months

Underperform (3): Stock is expected to achieve a total negative return of at least 10% over the next 12 months

Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

Outperform (1): Stock expected to outperform the S&P 500

Neutral (2): Stock expected to perform in line with the S&P 500

Underperform (3): Stock expected to underperform the S&P 500

Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

Cowen Securities, formerly known as Dahlman Rose & Company, Rating System until May 25, 2013

Buy – The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market return

Sell – The fundamentals/valuations of the subject company are deteriorating and the investment return is expected to be 5 to 15 percentage points lower than the general market return

Hold – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

Cowen And Company Rating Definitions

Distribution of Ratings/Investment Banking Services (IB) as of 06/30/14

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	417	58.57%	94	22.54%
Hold (b)	279	39.19%	7	2.51%
Sell (c)	16	2.25%	0	0.00%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

Note: "Buy", "Hold" and "Sell" are not terms that Cowen and Company, LLC uses in its ratings system and should not be construed as investment options. Rather, these ratings terms are used illustratively to comply with FINRA and NYSE regulations.

Loxo Oncology Rating History as of 09/01/2014
powered by: BlueMatrix

Relypsa Rating History as of 09/01/2014
powered by: BlueMatrix

Sunesis Pharmaceuticals Rating History as of 09/01/2014
powered by: BlueMatrix

Rating Change - 2/21/2006 - Outperform Rating

Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | $xx = Price Target | NA = Not Available | S=Suspended

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