Loxo Oncology, Inc. (LOXO)

Journal Article Describes Partial Response in First TRK Patient Treated with LOXO-101

MARKET OUTPERFORM | Price: $16.58 | Target Price: $23.00

MARKET DATA

Price	$16.58
52-Week Range:	$9.90 - $21.48
Shares Out. (M):	16.6
Market Cap ($M):	$275.2
Average Daily Vol. (000):	54.0
Cash (M):	$108
Cash/Share:	$6.47
Enterprise Value (M):	$212
Float (M):	16.2
LT Debt (M):	$0

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2014A	2015E	2016E
Revenue ($M)	1Q	$0.0	$0.0A	--
	2Q	$0.0	$0.0	--
	3Q	$0.0	$0.0	--
	4Q	$0.0	$0.0	--
	FY	**$0.0**	**$0.0**	**$0.0**
EPS	1Q	($0.68)	($0.38)A	--
	2Q	($14.39)	($0.41)	--
	3Q	($0.68)	($0.48)	--
	4Q	($0.57)	($0.51)	--
	FY	**($3.06)**	**($1.78)**	**($3.42)**

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

INVESTMENT HIGHLIGHTS

Loxo Oncology announced publication of a clinical response seen with the first TRK-positive patient treated with LOXO-101; reiterate our Market Outperform rating and $23 price target derived through a synthesis of discounted cash flow, sum-of-the-parts, and compound annual growth valuation methodologies. Yesterday, Loxo Oncology reported in a research brief in *Cancer Discovery* the early results from the first cancer patient harboring a TRK (tropomyosin receptor kinase) fusion, treated with LOXO-101. Recall, LOXO-101 is a selective TRK inhibitor licensed from Array BioPharma (ARRY, NC). After four months of dosing with 100 mg of twice daily LOXO-101, the female patient's tumors (metastatic lung lesions arising from soft tissue sarcoma) appear to have regressed substantially (Figure 2). Importantly, no drug-related adverse events were noted, and the tumor response observed was also accompanied by improvement in breathing (in pulmonary dyspnea and oxygen saturation). While the results are representative of short-term data from only a single patient from the Phase I dose-escalation trial of LOXO-101 as monotherapy, the positive results demonstrate validation of target, in our view.

N=1, but encouraging validation of target. As a reminder, LOXO-101 is being evaluated in an open-label, multicenter Phase I dose-escalation trial in patients with advanced solid tumors, where patients are being dosed once or twice daily in continuous 28-day cycles. The results announced yesterday represent analysis from the first identified TRK-positive patient in the study. Using Foundation Medicine's (FMI, NC) FoundationOneHeme panel (a multi-target comprehensive genomic profiling assay), this 41-year old female patient with a rare form of advanced cancer (soft tissue sarcoma widely metastatic to the lungs) was identified as possessing an *LMNA-NTRAK1* fusion gene, as well as a loss of the tumor suppressor *CDKN2A/B*, but harboring no other known oncogenic mutations. Like many other gene fusions, such as ALK and ROS1, TRK fusions are oncogenic drivers that have been shown to drive tumor growth and engage key cancer-related downstream signaling pathways as MAPK and AKT (Figure 3). TRK fusions are not common in soft tissue sarcoma, which are typically treated with single-agent doxorubicin, which has historically generated a response rate of ~20%. Although the result is preliminary, the rapid clinical tumor regression observed with the patient provides preliminary validation that NTRK1 fusion is a molecular driver of the patient's disease that could be directly targeted with LOXO-101. We note that additional patients harboring TRK fusions will have to be treated with LOXO-101 to further validate this initial finding.

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Keeping TRK. While we note that caution must be drawn when making comparisons, given the different tumor types being tested, we recognize that investors are likely to draw comparisons between LOXO-101 and Ignyta's (RXDC, NC) inhibitor, entrectinib (inhibitor of NTRK1/2/3, ROS1, ALK fusions), which has also shown preliminary encouraging results with TRK patients (Figure 4). Given the recent results, we continue to believe LOXO-101 is potentially a superior candidate given its high specificity to TRK isoforms and limited exposure to the CNS. Accordingly, there were no adverse events attributable to LOXO-101. While entrectinib has been well tolerated in patients, two DLTs (dose limiting toxicities), although reversible, have been observed with daily dosing of the regimen.

Quick refresher on TRK and LOXO-101. Recall that the TRK family of neurotrophin receptors, exemplified by TRKA, TRKB and TRKC, function primarily in the growth, differentiation and survival of neurons. NTRK1 fusions have been described in a subset of lung adenocarcinoma patients; and more recently, TRK fusions were found in many more tumor types than previously elucidated (see our Note from Last November), suggesting a broader market potential for LOXO-101. The compound binds all three subtypes of the TRK receptors, i.e., TRKA, B, and C. LOXO-101 is being developed under license from Array BioPharma (ARRY, NC), and is undergoing clinical development in patients with advanced solid tumors.

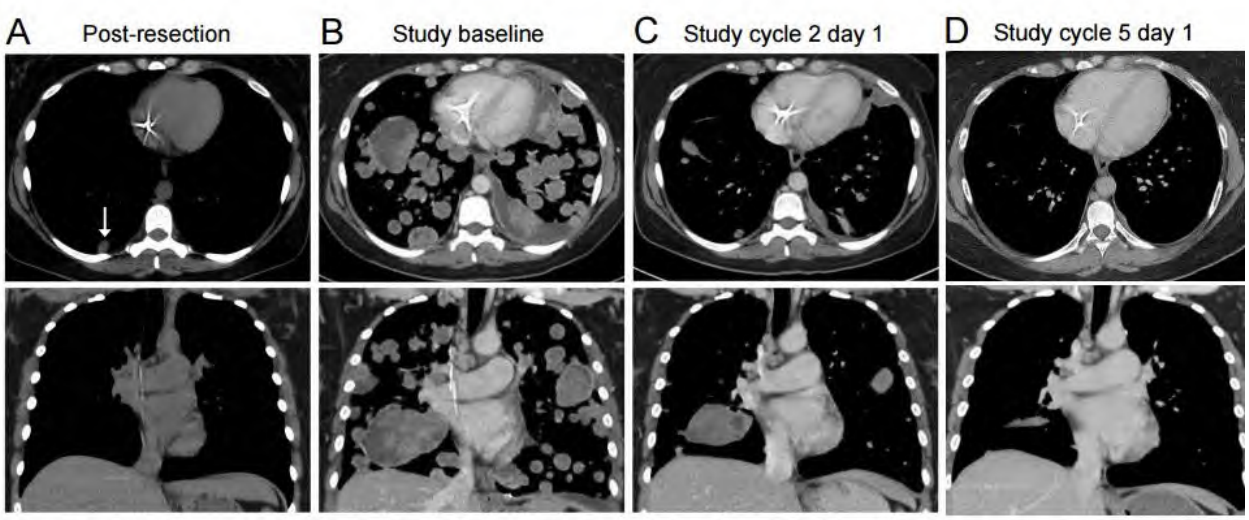
We believe an investment in LOXO represents an investment in a modern model of the oncology drug development company. More concretely, we believe LOXO-101 represents a compound with a high likelihood of clinical benefit and, ultimately, regulatory and commercial success. In our view, LOXO-101 should generate $1 billion-plus worldwide revenues, divided amongst three separate indications (NSCLC, mCRC and papillary thyroid cancer). Longer term, we believe the management team, with guidance and input from its highly-experienced scientific advisory board, possesses the necessary skill set to repeat the success that we expect to be achieved with LOXO-101 with future pipeline candidates.

FIGURE 1. Upcoming Milestones

Timing	Catalyst
2H15	Complete dose escalation portion of Phase I study with LOXO-101
2H15	Potential to present additional LOXO-101 clinical data
2H15	Present preclinical data at a medical meeting of other pipeline programs

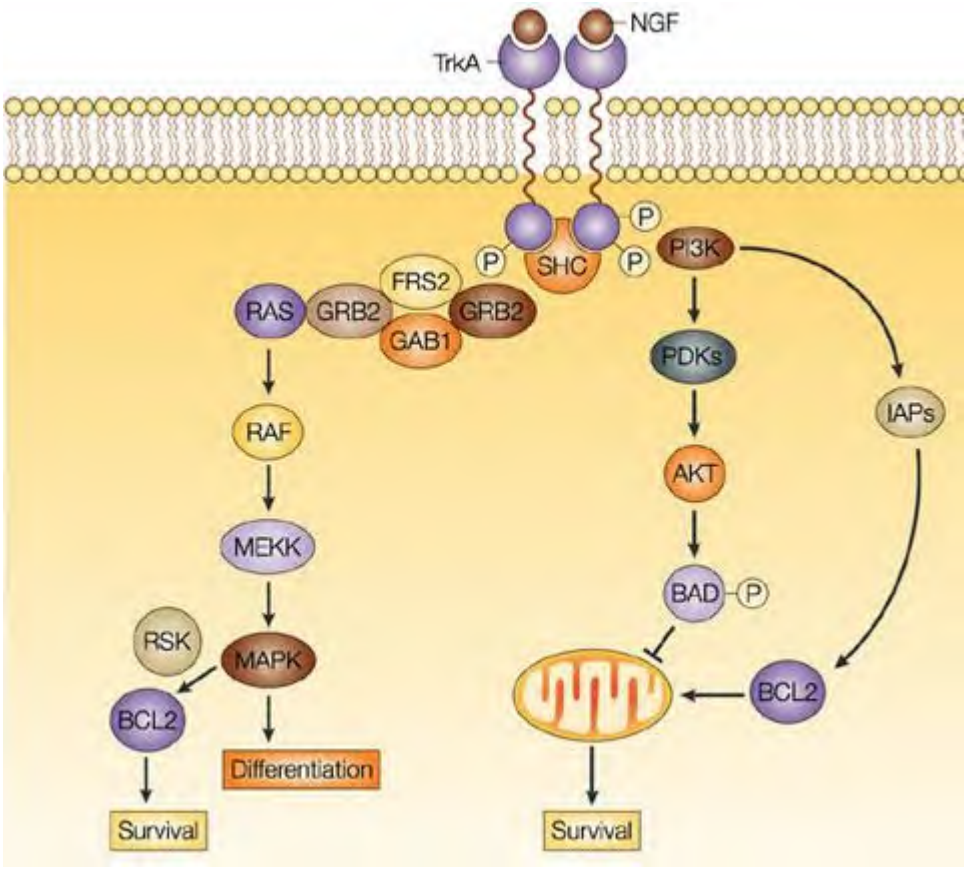
Source: JMP Securities LLC and Company Reports

FIGURE 2. Radiologic Response to LOXO-101



Source: Doebele et al. 2015

FIGURE 3. Signal Transduction of the TrkA Tyrosine Kinase Receptor



Source: Brodeur 2003

FIGURE 4. Early Results with TRK Inhibitors

	Gene	Gene Fusion	Study	Tumor Type	Dose (mg/m^2)	Best Response	Prior Therapies
LOXO	NTRK1	*LMNA-NTRK1*		STS	100 BID	PR	sorafenib, epirubicin/ifosfamide/mesna, radiation, surgery, doxorubicin
RXDX	NTRK3	*ETV6-NTRK3*	ST-1	Acinic Cell	400 QD	PR	surgery/EBRT,vinorelbine,carboplatin/ paclitaxel, additional surgery, doxorubicin,
	NTRK1/2/3*		ALKA	CRC	1600 Sch A	PR**	
	NTRK1	*SQSTM1-NTRK1*	ST-1	NSCLC	400 QD	PR	carboplatin/pemetrexed,pembrolizumab,docetaxel, vinorelbine

*gene mutation unknown
**PD

Source: JMP Securities LLC and Company Reports

FIGURE 5. Updated Income Statement

LOXO Oncology (LOXO)	2014A	1Q15A	2Q15E	3Q15A	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E
Income Statement ($MM)	2014A	1Q15A	2Q15E	3Q15A	4Q15E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E
Product Sales and Royalties:																				
LOXO-101																				
US Sales						-	-	-	99.9	203.1	316.6	457.0	576.8	637.1	685.5	714.7	742.3	770.9	800.7	831.5
ROW Royalties						-	-	-	-	14.1	36.8	59.8	82.9	106.0	124.1	134.3	138.0	139.7	141.4	143.2
Total Product Sales and Royalties	-	-	-	-	-	-	-	-	99.9	217.3	353.4	516.8	659.7	743.2	809.7	849.0	880.3	910.6	942.1	974.7
Collaboration Revenue	-					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Total Revenue	-	-	-	-	-	-	-	-	99.9	217.3	353.4	516.8	659.7	743.2	809.7	849.0	880.3	910.6	942.1	974.7
Cost of Goods Sold							-	-	12.0	24.4	38.0	54.8	69.2	76.5	82.3	85.8	89.1	92.5	96.1	99.8
Gross Profit	-	-	-	-	-	-	-	-	87.9	192.9	315.4	462.0	590.5	666.7	727.4	763.2	791.2	818.1	846.0	874.9
Operating Expenses:																				
Research and development with related party	7.568	1.9	2.2	2.4	2.6	9.1	10.2	10.7	11.3	11.8	11.8	11.8	11.8	11.8	11.8	11.8	11.8	11.8	11.8	11.8
Research and development	6.947	1.9	2.2	2.5	2.7	9.3	18.6	37.3	59.6	71.5	78.7	82.6	86.8	91.1	93.8	96.6	99.5	102.5	105.6	108.8
General and administrative	6.175	2.4	2.3	2.4	2.5	9.6	16.8	27.7	44.3	62.0	74.4	85.6	92.5	98.0	102.9	105.0	107.1	109.2	111.4	113.6
Milestone Expense to ArrayBiopharm							10.0	10.0	25.0	10.0	10.0	10.0	10.0							
Total operating expenses	20.690	6.225	6.7	7.3	7.8	28.0	55.6	85.7	140.2	155.4	175.0	190.1	201.0	200.9	208.6	213.4	218.4	223.6	228.8	234.2
Operating income (loss)	(20.690)	(6.225)	(6.7)	(7.3)	(7.8)	(28.0)	(55.6)	(85.7)	(52.2)	37.5	140.4	271.9	389.5	465.8	518.8	549.8	572.8	594.5	617.2	640.7
Operating margin (%)									*-52.3%*	*17.3%*	*39.7%*	*52.6%*	*59.0%*	*62.7%*	*64.1%*	*64.8%*	*65.1%*	*65.3%*	*65.5%*	*65.7%*
Other income (expense):																				
Interest income	0.018	0.043				0.0														
Interest expense																				
Total other income, net	0.018	0.0	-	-	-	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Pretax incomee (loss)	(20.672)	(6.182)	(6.7)	(7.3)	(7.8)	(28.0)	(55.6)	(85.7)	(52.2)	37.5	140.4	271.9	389.5	465.8	518.8	549.8	572.8	594.5	617.2	640.7
Comprehensive income (loss)						0.0	0.0	0.0	0.0	(1.9)	(14.0)	(54.4)	(116.8)	(163.0)	(181.6)	(192.4)	(200.5)	(208.1)	(216.0)	(224.2)
Tax Rate										*5%*	*10%*	*20%*	*30%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
Comprehensive income (loss)	(20.672)	(6.2)	(6.7)	(7.3)	(7.8)	(28.0)	(55.6)	(85.7)	(52.2)	35.6	126.4	217.5	272.6	302.8	337.2	357.4	372.3	386.5	401.2	416.5
Accretion of redeemable convertible preferred stock	-0.034																			
Net income (loss) attributable to common stockholders	(20.706)	(6.2)	(6.7)	(7.3)	(7.8)	(28.0)	(55.6)	(85.7)	(52.2)	35.6	126.4	217.5	272.6	302.8	337.2	357.4	372.3	386.5	401.2	416.5
Basic EPS to common shareholders	**$ (3.06)**	$ (0.38)	$ (0.41)	$ (0.48)	$ (0.51)	**$ (1.78)**	**$ (3.42)**	**$ (4.58)**	**$ (2.47)**	**$ 1.62**	**$ 5.58**	**$ 9.29**	**$ 11.28**	**$ 12.15**	**$ 13.14**	**$ 13.52**	**$ 13.69**	**$ 13.82**	**$ 13.96**	**$ 14.11**
Diluted EPS to common shareholders	**$ (3.06)**	$ (0.38)	$ (0.41)	$ (0.48)	$ (0.51)	**$ (1.78)**	**$ (3.42)**	**$ (4.58)**	**$ (2.47)**	**$ 1.25**	**$ 4.32**	**$ 7.24**	**$ 8.84**	**$ 9.57**	**$ 10.40**	**$ 10.76**	**$ 10.94**	**$ 11.10**	**$ 11.26**	**$ 11.43**
Basic shares outstanding	6.8	16.5	16.5	15.1	15.2	15.7	16.3	18.7	21.2	21.9	22.7	23.4	24.2	24.9	25.7	26.4	27.2	28.0	28.7	29.5
Diluted shares outstanding	6.8	16.5	16.5	15.1	15.2	15.7	16.3	18.7	21.2	28.5	29.3	30.1	30.8	31.6	32.4	33.2	34.0	34.8	35.6	36.4

Source: JMP Securities LLC and Company Reports

Company Description

Loxo Oncology, based in Stamford, CT, is a biotechnology company focused on the development of targeted, small molecule therapeutics for the treatment of cancer in genetically defined patient populations. By focusing on the engagement molecular targets exhibiting the hallmarks of oncogene addiction, Loxo aims to maximize the probability of clinical success while reducing the time, cost, and risks associated with drug development.

The company's lead product candidate, LOXO-101, is a potent selective inhibitor of tropomyosin receptor kinase (Trk), currently in a Phase I dose escalation trial, expected to give a preliminary safety and PK/PD read-out in early 2015. Trk comprises a family of membrane-bound signaling molecules that, when aberrantly expressed through genetic alterations, play an important role in the pathogenesis of various cancers. The company also intends to expand its pipeline with additional small molecule inhibitors targeting cancers driven by specific genetic alterations, nominating a new candidate in 1H15.

Investment Risks

Potential risks to our price target include, but are not limited to, clinical, regulatory, commercial and competitive factors.

Clinical. Drug development is an inherently risky business. Like all clinical trials, LOXO-101 clinical development carries some risk of failure. LOXO-101 may fail to maintain the requisite safety or demonstrate meaningful efficacy to warrant further development through to regulatory approval.

Regulatory and commercial. The ability of Loxo or its future potential partners to market its drugs depends on those drugs obtaining approval from the FDA and foreign regulatory agencies. Failure to achieve approval or delays in the timelines to approval could negatively impact the company’s share price.

Competitive. Oncology drug development is an increasingly competitive field. Loxo faces competition from companies developing existing small molecule agents that target the Trk family of kinases, and agents inhibiting cancer-related mechanisms of action applicable to intended indications with LOXO-101. Some of the companies may have access to greater resources and expertise compared to Loxo Oncology.

Partnering. The development of LOXO-101 and additional candidate programs is governed, in part, by a multi-year strategic collaboration agreement with Array BioPharma (ARRY), wherein Loxo has been granted access to Array’s compound library and chemistry platform. Changes to this collaboration agreement could have a substantially negative impact on Loxo’s ability to expand its pipeline and, in turn, valuation.

Financial. Taking into account ~$60MM in net proceeds raised through its IPO, we estimate that Loxo will finish 3Q and FY2014 with cash and cash equivalents of $79MM and $75MM, respectively, which we believe should be adequate resources to fund operations into 1H17. We anticipate that Loxo will seek additional equity financing in the form of a secondary offering in order to complete the development of LOXO-101 and advance its future pipeline candidates, exposing existing shareholders to some degree of dilution risk.

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Market Outperform (MO): JMP Securities expects the stock price to outperform relevant market indices over the next 12 months.
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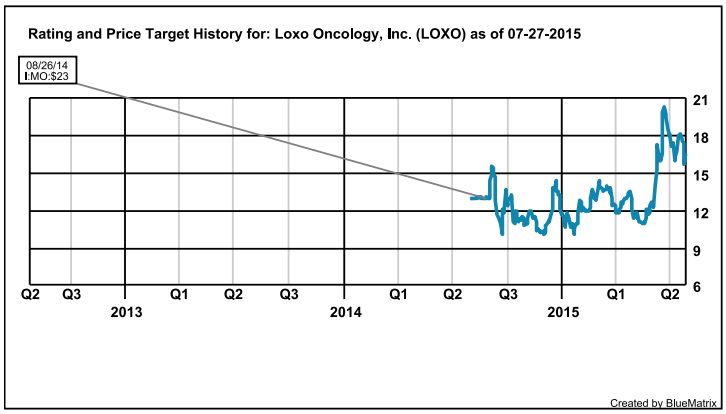
JMP Rating	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	Regulatory Equivalent	# Co's Under Coverage	*% of Total*	# Co's Receiving IB Services in Past 12 Months	*% of Co's With This Rating*
MARKET OUTPERFORM	Buy	289	*62.69%*	Buy	289	*62.69%*	86	*29.76%*
MARKET PERFORM	Hold	143	*31.02%*	Hold	143	*31.02%*	16	*11.19%*
MARKET UNDERPERFORM	Sell	8	*1.74%*	Sell	8	*1.74%*	0	*0%*
COVERAGE IN TRANSITION		21	*4.56%*		21	*4.56%*	4	*19.05%*
TOTAL:		461	*100%*		461	*100%*	106	*22.99%*

Stock Price Chart of Rating and Target Price Changes:

Note: First annotation denotes initiation of coverage or 3 years, whichever is shorter. If no target price is listed, then the target price is N/A. In accordance with NASD Rule 2711, the chart(s) below reflect(s) price range and any changes to the rating or price target as of the end of the most recent calendar quarter. The action reflected in this note is not annotated in the stock price chart. Source: JMP Securities.



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