February 20, 2014

OUTPERFORM

Reason for report:

COMPANY UPDATE

Howard Liang, Ph.D.
(617) 918-4857
Howard.Liang@Leerink.com

Gena Wang, Ph.D., CFA
(212) 277-6073
Gena.Wang@Leerink.com

LEERINK

ONCONOVA THERAPEUTICS, INC.

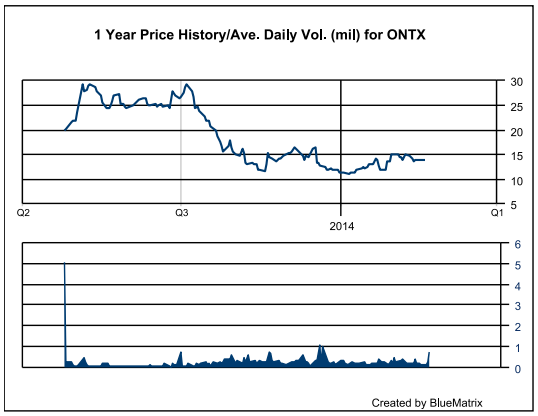
Lower-Risk MDS Opportunity Remains for Rigosertib Despite High-Risk Failure

• **Bottom Line:** Yesterday, OTNX reported negative top-line results from its Phase III ONTIME trial of IV rigosertib in 299 higher-risk myelodysplastic syndrome (MDS) patients who previously failed or relapsed after hypomethylating agents (HMAs). While a statistically significant improvement was seen in the subset of patients who did not respond to HMAs, we believe it is appropriate for the focus to shift to the lower-risk MDS setting for which we expect an FDA-agreed trial design to be announced shortly and a Phase III could proceed relatively quickly. We believe the failure in the higher-risk patient population does not necessarily predict the outcome in the lower-risk setting in part due to differences in endpoints (overall survival vs. transfusion independence). Despite controversy, we believe available data show activity for rigosertib in this population that is independent of ESA. While we are mindful of the binary nature of the lower-risk Phase III readout, we believe the more attractive commercial opportunity in the lower-risk MDS setting with an oral agent that has shown a good tolerability profile and potentially greater transferability of Phase II data based on the same endpoint (transfusion independence) makes it a worthwhile investment at current valuations. We are lowering our price target from $37 to $14 assuming only probability-weighted opportunities in lower-risk MDS.

• **In our opinion, rigosertib Phase II data for lower-risk MDS are better than in higher-risk MDS.** Transfusion independence, which is highly likely to be primary endpoint of the Phase III in lower-risk MDS patients, has been observed compared to bone marrow response in higher-risk patients, which is of unknown significance. In the ONTARGET Phase II trial, rigosertib produced transfusion independence responses in patients who were previously transfusion-dependent. Furthermore, these responses did not appear to be correlated with the timing of erythropoietin-stimulating agent (ESA) administration (LINK). The question will be primarily whether the magnitude of the transfusion independence is robust enough and clinically meaningful. Based on the relatively large size (e.g., nearly 400) of other lower-risk MDS trials with transfusion independence as the primary endpoint, it would appear that the targeted effect size may not be especially large. We expect the company to report the design of the Phase III trial in this population imminently and would anticipate faster accrual and completion of this trial compared with ONTIME, given that overall survival is not an endpoint.

Key Stats:	**(NASDAQ:ONTX)**
S&P 600 Health Care Index:	**1,296.99**
Price:	**$13.86**
Price Target:	$14.00 from $37.00
Methodology:	DCF analysis
52 Week High:	$31.13
52 Week Low:	$10.80
Shares Outstanding (mil):	21.5
Market Capitalization (mil):	$298.0
Book Value/Share:	$4.51
Cash Per Share:	$5.44
Dividend (ann):	$0.00
Dividend Yield:	0.0%

General: as of the end of 3Q13



Dec Yr	1Q	2Q	3Q	4Q	FY Rev	1Q	2Q	3Q	4Q	FY EPS	P/E
2012A	--	--	--	--	$46.2	--	--	--	--	($2.67)	NM
2013E - New	**$1.1A**	**$0.6A**	**$1.1A**	**$1.1**	**$3.9**	**($1.03)A**	**($0.64)A**	**($0.97)A**	**($0.95)**	**($3.54)**	**NM**
2013E - Old	$1.1A	$0.6A	$1.1A	$1.1	$3.9	($1.03)A	($0.64)A	($0.97)A	($0.94)	($3.54)	NM
2014E - New	**--**	**--**	**--**	**--**	**$27.1**	**--**	**--**	**--**	**--**	**($2.36)**	**NM**
2014E - Old	--	--	--	--	$2.1	--	--	--	--	($4.35)	NM

Source: Company Information and Leerink Partners LLC Research
Revenues in millions; EPS are GAAP.

INVESTMENT THESIS

ONTX is a late-stage story, with a Phase III trial in low-risk myelodysplastic syndrome (MDS) expected to begin in 2014. Although the IV formulation of rigosertib failed to show a statistically significant overall survival benefit in its Phase III ONTIME trial in higher-risk MDS, the numerical trend toward improvement in survival in the overall trial, along with a significant survival benefit in a post-hoc analysis of hypomethylating-agent refractory patients, suggests that the drug does have some activity. While we do not expect the company to attempt another trial in the higher-risk population, we believe oral rigosertib's opportunity in lower-risk MDS should be viewed independent of the outcome of ONTIME. In contrast to the higher-risk setting, more robust hematological responses such as transfusion independence were seen. MEDACorp key opinion leaders view rigosertib data in lower-risk patients to be stronger than in higher-risk MDS. ONTX is one of a minority of biotech companies that have been able to maintain full US rights to their lead compound near the finish line.

Secondary endpoints will provide additional clarity on the efficacy signal in higher-risk MDS. The median overall survival in the rigosertib + best supportive care (BSC) arm was 8.2 months, compared to 5.8 months in BSC-only arm (HR: 0.86; p=0.27). In a post-hoc analysis of 184 patients who had not responded to HMA (either failed or progressed while on treatment), there was a significant improvement in survival in favor of the rigosertib arm (8.5 months vs. 4.7 months; HR=0.67; p=0.022). It appears unlikely that the company will conduct another Phase III study in this subgroup, which we would view to be the right decision given the hazards of post-hoc analyses. Nonetheless, psychologically this provides some comfort that there is some activity. ONTX did not provide any data from the secondary endpoints in the trial, which include bone marrow response, hematological improvement, and transition time to acute myeloid leukemia (AML), but indicated these would be made available in a late-breaking abstract at the American Society of Clinical Oncology (ASCO) annual meeting, or perhaps earlier, following discussions with the FDA. If these endpoints show at least a trend toward improvement with rigosertib, this could further strengthen the case for the activity of the drug in MDS.

IV rigosertib looks very safe and tolerable. The company reported a similar profile of serious adverse events in both study arms, with Grade 3/4 treatment-related hematologic and non-hematologic AEs in less than 7% and 3% of patients, respectively. Treatment-related adverse events occurring in more than 10% of patients included nausea (22%), diarrhea (17%), fatigue (17%), and constipation (15%). While the oral formulation has been shown to have a different tolerability profile (including higher rates of urinary toxicity, which have been mitigated using a lower dose), it is nonetheless comforting that no serious safety signals were seen.

Update to model. We assume no further development in the higher-risk population and remove all forecasts for this indication from our model. We continue to assume a 50% probability that oral rigosertib is launched in early 2017 and forecast SG&A to remain flat until then. As a result, we are lowering our price target to $14 from $37.

VALUATION

We are lowering our 12-month valuation on ONTX shares to $14 from $37 based on DCF methodology. We assume rigosertib launches in lower-risk MDS in 2017 and no further development in higher-risk MDS. Our royalty assumption is 12-19% for ex-US sales. Our projection for peak penetration is 25% for lower-risk MDS. Our projection for probability-weighted (50% for lower-risk MDS) sales of rigosertib reaches $161M for US, and ex-US royalties reach $31M by 2029. We use a discount rate of 10%, which we believe is appropriate given the probability-weighted sales projection.

RISKS TO VALUATION

Risks to our valuation include the following:

Binary clinical risk with Phase III readout of rigosertib in lower-risk MDS.

Commercial and execution risks as a small company.

Financing risk – ONTX has estimated pro forma cash of ~$110M, which together with anticipated milestone payment we estimate to be sufficient to fund operations into 2015, and the company may have additional financing needs before turning cash flow positive.

ONTX Income Statement ($000)	2011A	2012A	Mar-13A	Jun-13A	Sep-13A	Dec-13E	2013E	2014E	2015E	2016E	2017E	2018E
Collaboration agreements/Milestones								25,000	25,000	50,000	50,000	
Royalties									0	0	2,411	9,234
Sales									0	0	37,098	97,719
Total revenue	1,487	46,190	1,116	591	1,116	1,116	3,939	27,116	25,000	50,000	89,509	106,954
COGS										4,000	7,161	7,818
% of revenue										*8%*	*8%*	*8%*
R&D	22,624	52,762	12,756	10,047	15,293	15,446	53,542	54,039	50,620	52,139	53,703	55,314
SG&A	6,436	15,707	3,346	3,117	5,927	5,986	18,376	24,000	24,000	34,000	54,000	56,700
Total operating expenses	29,060	68,469	16,102	13,164	21,220	21,432	71,918	78,039	74,620	90,139	114,864	119,832
Net income (loss) from operations	(27,573)	(22,279)	(14,986)	(12,573)	(20,104)	(20,316)	(67,979)	(50,923)	(49,620)	(40,139)	(25,355)	(12,878)
Change in fair value of warrant liability	1,287	367	14	(2)	(31)	0	(19)					
Interest expense	(19)	(8,608)	0	(2)	(1)	0	(3)					
Other income, net	11	608	127	15	47	0	189	0	0	0	0	0
Net income (loss) before income taxes	(26,294)	(29,912)	(14,845)	(12,562)	(20,089)	(20,316)	(67,812)	(50,923)	(49,620)	(40,139)	(25,355)	(12,878)
Provision (benefit) for income taxes	0	0	0	0	432	0	432	0	0			
Tax rate												
Net income (loss)	(26,294)	(29,912)	(14,845)	(12,562)	(20,521)	(20,316)	(68,244)	(50,923)	(49,620)	(40,139)	(25,355)	(12,878)
Accretion of preferred stock	(4,020)	(3,953)	(1,019)	(1,032)	(269)	0	(2,320)	0	0			
Net income (loss) to common stockholders	(30,314)	(33,865)	(15,864)	(13,594)	(20,790)	(20,316)	(70,564)	(50,923)	(49,620)	(40,139)	(25,355)	(12,878)
Net loss per share	**(14.18)**	**(2.67)**	**(1.03)**	**(0.64)**	**(0.97)**	**(0.95)**	**(3.54)**	**(2.36)**	**(1.55)**	**(1.23)**	**(0.66)**	**(0.33)**
Basic shares	2,137	12,669	15,446	21,389	21,404	21,446	19,921	21,554	31,985	32,625	38,277	39,043
Dilutive shares			15,446	24,186	24,428	24,672	22,183	25,295	35,548	37,326	44,192	46,401

Source: Company Reports and Leerink Partners estimates

Disclosures Appendix

Analyst Certification

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

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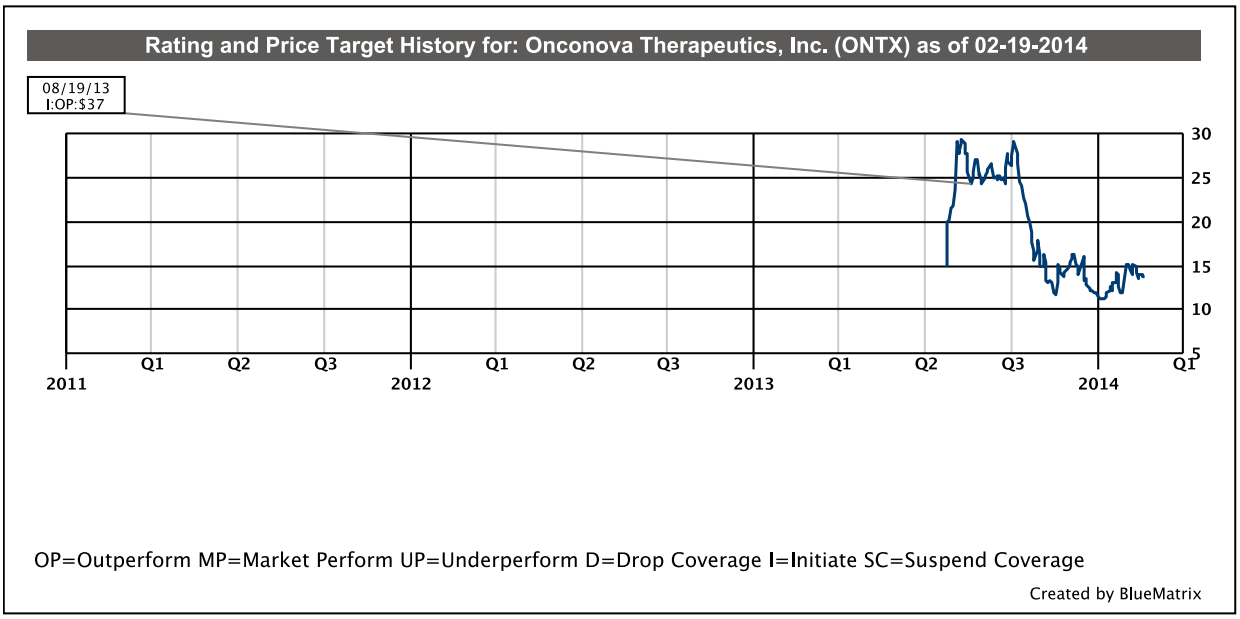

Distribution of Ratings/Investment Banking Services (IB) as of 12/31/13				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	118	64.50	30	25.00
HOLD [MP]	65	35.50	2	3.00
SELL [UP]	0	0.00	0	0.00

Explanation of Ratings

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

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

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

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

Important Disclosures

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Leerink Partners LLC makes a market in Onconova Therapeutics, Inc.

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

Leerink Partners LLC Equity Research

Director of Equity Research	**John L. Sullivan, CFA**	(617) 918-4875	john.sullivan@leerink.com
Associate Director of Research	**Alice C. Avanian, CFA**	(617) 918-4544	alice.avanian@leerink.com
Healthcare Strategy	**John L. Sullivan, CFA**	(617) 918-4875	john.sullivan@leerink.com
	Alice C. Avanian, CFA	(617) 918-4544	alice.avanian@leerink.com
Biotechnology	**Howard Liang, Ph.D.**	(617) 918-4857	howard.liang@leerink.com
	Joseph P. Schwartz	(617) 918-4575	joseph.schwartz@leerink.com
	Marko Kozul, M.D.	(415) 905-7221	marko.kozul@leerink.com
	Michael Schmidt, Ph.D.	(617) 918-4588	michael.schmidt@leerink.com
	Jonathan Chang, Ph.D.	(617) 918-4015	jonathan.chang@leerink.com
	Irene Lau	(415) 905-7256	irene.lau@leerink.com
	Paul Matteis	(617) 918-4585	paul.matteis@leerink.com
	Gena Wang, Ph.D., CFA	(212) 277-6073	gena.wang@leerink.com
Life Science Tools and Diagnostics	**Dan Leonard**	(212) 277-6116	dan.leonard@leerink.com
	Justin Bowers, CFA	(212) 277-6066	justin.bowers@leerink.com
Pharmaceuticals/Major	**Seamus Fernandez**	(617) 918-4011	seamus.fernandez@leerink.com
	Ario Arabi	(617) 918-4568	ario.arabi@leerink.com
Specialty Pharmaceuticals, Generics	**Jason M. Gerberry, JD**	(617) 918-4549	jason.gerberry@leerink.com
	Christopher W. Kuehnle, JD	(617) 918-4851	chris.kuehnle@leerink.com
Medical Devices, Cardiology & Orthopedics	**Danielle Antalffy**	(212) 277-6044	danielle.antalffy@leerink.com
	Richard Newitter	(212) 277-6088	richard.newitter@leerink.com
	Robert Marcus, CFA	(212) 277-6084	robert.marcus@leerink.com
	Ravi Misra	(212) 277-6049	ravi.misra@leerink.com
Healthcare Services	**Ana Gupte, Ph.D.**	(212) 277-6040	ana.gupte@leerink.com
Healthcare Technology & Distribution	**David Larsen, CFA**	(617) 918-4502	david.larsen@leerink.com
	Christopher Abbott	(617) 918-4010	chris.abbott@leerink.com
Sr. Editor/Supervisory Analyst	**Mary Ellen Eagan, CFA**	(617) 918-4837	maryellen.eagan@leerink.com
Supervisory Analysts	Robert Egan		bob.egan@leerink.com
	Amy N. Sonne		amy.sonne@leerink.com

New York
299 Park Avenue, 21st floor
New York, NY 10171
(888) 778-1653

Boston
One Federal Street, 37th Floor
Boston, MA 02110
(800) 808-7525

San Francisco
201 Spear Street, 16th Floor
San Francisco, CA 94105
(800) 778-1164