December 20, 2013

OUTPERFORM

Reason for report:

FLASH NOTE

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

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

LEERINK SWANN

HEALTHCARE EQUITY RESEARCH

ONCONOVA THERAPEUTICS, INC.

Analyst Meeting Highlights Broad Program for Rigosertib and Near-Term Readout

Key Stats:	(NASDAQ:ONTX)
S&P 600 Health Care Index:	1,251.31
Price:	$13.48
52 Week High:	$31.13
52 Week Low:	$11.73
Shares Outstanding (mil):	2.6
Market Capitalization (mil):	$35.1

• **Bottom Line:** ONTX held an analyst meeting yesterday that highlighted a relatively broad program for lead compound rigosertib in over 1,000 patients and rigorously designed clinical studies , which we find noteworthy for a company the size of ONTX. Our incremental takeaways include the timing of ONTIME Phase III data for rigosertib in higher-risk MDS (likely in early part of 1Q:14), status and plans for lower-risk MDS setting, as well as new information on the mechanism of action of rigosertib. While the upcoming rigosertib ONTIME data clearly represent a binary event, we believe risk / reward is favorable at current levels due to what we view to be significantly potentially higher upside vs. downside.

• **ONTIME readout drawing close, data as early as January.** Phase III trial comparing IV rigosertib plus best supportive care (BSC) with BSC (2:1 randomization) in ~300 higher-risk MDS patients (vs. 270 planned) who have failed a hypomethylating agent (Vidaza or Dacogen). The study was conducted in 89 sites worldwide (42 US), started enrollment in Dec 2010, and completed in May 2013. The trial was designed with >90% power to detect a significant difference in overall survival (OS), assuming an OS of approximately four months for the control group and a difference of 10 to 13 weeks between the two arms. There had been several safety looks by the Data Safety Monitoring Board (DSMB) but there is no futility or interim efficacy look per trial design. Although it is unknown whether bone marrow response seen with rigosertib can lead to survival benefit, we believe the trial design of essentially placebo as the comparator is favorable as we do not expect a meaningful impact from low-dose ara-C.

• **Rigosertib responses in lower-risk patients occur regardless of concurrent ESA use or prior ESA failure.** Dr. Azra Raza of Columbia University provided a recap of the Phase II oral rigosertib data in lower-risk MDS patients presented the American Society of Hematology (ASH) conference last week, explaining that the drug was able to induce transfusion dependence in both alone and in combination with erythropoietin stimulating agents (ESAs). There was a 44% response rate among patients deemed ESA-resistant, versus 0% in 5 patients who had no prior ESA therapy. By comparison, Dr. Raza noted hypomethylating agents produce an approximately 17% response rate in ESA-resistant patients. Additionally, she highlighted the reduction in urinary toxicity that was achieved by lowering the dose (from 560 mg BID to 560 mg in the morning and 280 mg in the afternoon) and encouraging patients to drink plenty of fluids. Only one of thirteen patients receiving the new dose developed a grade 2 urinary toxicity, compared with 43% grade 2 and 11% grade 3 toxicities seen in the original dosing schedule. Rigosertib responses were also correlated with particular methylation profiles, which ONTX hopes to verify prospectively as a predictive biomarker in future trials. The company has a meeting set up with the FDA and will update the Street after the meeting with its plan on how to move forward in lower-risk MDS and considerations for a Phase III in this setting.

• **Rigosertib appears to inhibit Plk-1 and PI3K indirectly though the inactivation of Ras.** At the analyst day, Dr. Premkumar Reddy of Mount Sinai and scientific founder on Onconova presented new

data on rigosertib's mechanism of action. While the drug had been previously identified as both a Plk-1 and PI3K inhibitor, Dr. Reddy explained that rigosertib binds to a specific Ras binding site which keeps Ras in an inactivated state and prevents it binding to and activating Raf. In the absence of activated Raf, both Plk-1 and the PI3K pathways are shut down. This differs from the mechanism of Boehringer-Ingelheim's volasertib, which binds directly to Plk-1. Volasertib has shown encouraging activity and is in Phase III for AML, which is a disease with similarities to MDS. Dr. Reddy suggested that this direct inhibition leads to the severe myelosuppression seen in mice treated with volasertib, but not seen in those treated with rigosertib. Many other pathways also rely on the Ras binding domain, and the effect of rigosertib on these is also being explored. It is currently unclear how this is correlated with the methylation signature seen in rigosertib responders with lower-risk disease. Dr. Raza suggested there may be an association between Ras signaling and epigenetics, but this remains to be explored.

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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.

Valuation

Our 12-month valuation on ONTX shares is $37 based on DCF methodology. We assume rigosertib launches in higher-risk MDS in 2015 and in lower-risk MDS in 2017. Our royalty assumption is 12-19% for ex-US sales. Our projection for peak penetration is 30% for high-risk MDS and 25% for low-risk MDS. Our projection for probability-weighted (60% for higher-risk and 50% for lower-risk MDS) sales of rigosertib reaches $394M for US, and ex-US royalties reach $75M by 2029. We use a discount rate of 10%, which we believe is appropriate given the probability-weighted sales projection.

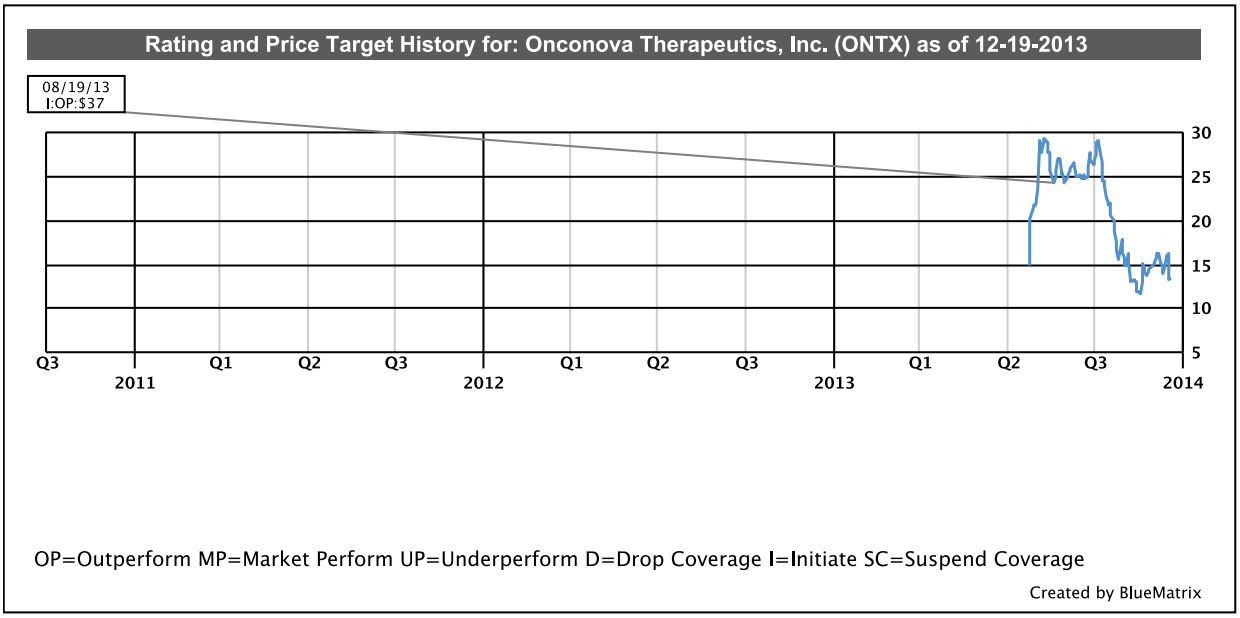
Risks to Valuation

Risks to our valuation include the following:

Binary clinical risk with Phase III readout of rigosertib in higher-risk MDS. Although Phase II demonstrated bone marrow response, full partial or complete responses by traditional definition were limited, and it is not clear that bone marrow response would predict survival benefit. In addition, although the survival observed in the Phase II compared favorably to historical control, such comparisons are difficult and have significant caveats.

Commercial and execution risks as a small company. The current continuous infusion dosing regimen for the IV formulation may present a challenge.

Financing risk – ONTX has estimated pro forma cash of ~$110M, which we estimate to be sufficient to fund operations through the end of 2014, and the company may have additional financing needs before turning cash flow positive.



Distribution of Ratings/Investment Banking Services (IB) as of 09/30/13				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	111	64.90	27	24.00
HOLD [MP]	60	35.10	0	0.00
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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In the past 12 months, the Firm has received compensation for providing investment banking services to Onconova Therapeutics, Inc.

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

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

Leerink Swann 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
	Irene Lau	(415) 905-7256	irene.lau@leerink.com
	Gena Wang, Ph.D., CFA	(212) 277-6073	gena.wang@leerink.com
	Paul Matteis	(617) 918-4585	paul.matteis@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