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## ONCOMED PHARMACEUTICALS, INC.

### Trial Halt a Setback, But Resumption Appears Likely

• **Bottom Line:** OMED voluntarily halted ongoing trials for its two Wnt programs – vantictumab (anti-Fzd7, OMP-18R5) and Fzd8-Fc (OMP-54F28) – due to bone-related adverse events (AEs). Currently, all patients are off the trial and the company plans to submit to the FDA an amendment for trial re-initiation at lower doses or less frequent dosing. Given relatively low event rates and activity seen at low doses, we believe the trials will likely be resumed with modified dosing and risk mitigation measures such as patient selection, prophylactic vitamin/calcium supplement and bone marker monitoring. The Wnt programs (partnered with Bayer) represent 2 of 5 clinical-stage programs for OMED. Since bone loss is a known on-target side effect for Wnt pathway, we do not believe there is read-through to other programs. Although a negative reaction to the news is understandable, we see upside to OMED shares with trial resumption and maintain our \$37 valuation for OMED.

• **On-target bone side effects were mild-to-moderate and across all doses.** Bone toxicity is an on-target side effect for inhibitors of Wnt pathway, which fosters bone formation and inhibits bone resorption. The observed bone-related adverse events were characterized as being mild-to-moderate, occurring in 8/63 patients (13%) for vantictumab, and 2/41 (5%) for OMP-54F28. OMED management noted that these involved fractures of small bones, with many captured during tumor assessment. Events occurred across all doses, and bone events appeared highly correlated with known risk factors (high  $\beta$ -CTX baseline or  $\beta$ -CTX doubling on trial).

• **Risk may be mitigated by a number of strategies.** After one reported Grade 3 compression fracture from the vantictumab early Phase I trial (at 0.5mg/kg q1w, after minor fall on Day 110), active risk mitigation has been implemented including more stringent exclusion criteria, prophylactic Vitamin D and calcium supplements, less frequent dosing, as well as zoledronic acid administration if  $\beta$ -CTX doubling (bone turnover marker) or T-score decline to  $<-2.5$  (measured by DEXA scan). Recent data presentation (ASCO 2014) for the OMP-54F28 Phase I trial showed only one Grade 2 bone event after 6 cycles of OMP-54F28 treatment at the highest dose tested (20mg/kg q3w).  $\beta$ -CTX doubling was observed in 6/26 patients, and reversed with zoledronic acid in 5/5 patients and no bone events. The new bone event occurred in the ongoing OMP-54F28 Phase Ib trials, with similar PK/PD profile to the previous event. Compared to the vantictumab program where 13% had bone-related AEs, OMP-54F28 had 1/26 (3%) bone-related event from the Phase I trial or 2/41 (5%) for the whole program. Initial risk mitigations seem to reduce bone-related AEs, and further optimization should improve bone-related tox profile.

• **Signs of activities were seen at the low doses.** So far, 3 prolonged stable diseases (SDs) were seen in the vantictumab Phase I trial in 3 patients with neuroendocrine tumors; all of them were at relatively low doses (0.5 mg/kg q1w, 0.5mg/kg q2w, and 1mg/kg q3w, compared to the highest of 15 mg/kg in the ASCO presentation). For the OMP-54F28 program, 9 patients experienced SD, with two patients (pancreatic and renal cell carcinoma) at 0.5 and 1mg/kg (q3w). Although lowering the

#### Key Stats:

(NASDAQ:OMED)

<b>S&amp;P 600 Health Care Index:</b>	<b>1,287.40</b>
<b>Price:</b>	<b>\$22.71</b>
52 Week High:	\$42.34
52 Week Low:	\$12.07
Shares Outstanding (mil):	29.4
Market Capitalization (mil):	\$667.7

dose may compromise activity to some extent, lower doses/less frequent dosing could still be well within the therapeutic window.

## Valuation

Our valuation is \$37 for OMED. We assume the demcizumab, anti-DLL4/VEGF program and the other 8 partner candidates launch in the front-line settings for pancreatic cancer, NSCLC (non-small cell lung cancer) and ovarian cancer in 2019-22 in the U.S. and in 2020-23 in the EU. Our royalty assumption is 12-15% for two Notch inhibitors, 12-16% for the first Wnt inhibitor, 5-10% for the second Wnt inhibitor, 10-15% for demcizumab, 5-13% for other four biologic candidates partnered with CELG. Our projection for peak penetration is 12% for NSCLC, 20% for pancreatic cancer, and 18% for ovarian cancer in the U.S. Our projection for probability-weighted (10%) sales for each asset reaches \$245M by 2030, two years after patent expiration. We also assign a 2X terminal value multiple to account for challenging generic entry for large molecule drugs. Our valuation is based on NPV and sum-of-the-part analysis using a discount rate of 10%, which we believe is appropriate given probability-weighted sales projection.

## Risks to Valuation

- Development risk – All of pipeline assets are still in early-stage clinical or preclinical development and they could fail at each development stage. OMED's agents have been all first-in-class. While this improved the upside upon success, the developmental risk may be higher.
- As therapies targeting cancer stem cells by design may only affect a small subpopulation of the tumor cells, observing an anti-tumor signal in early clinical development may be more challenging and demonstration of clinical efficacy may require a randomized study with a longer follow-up.
- Financing risk – OMED's cash could be sufficient to fund operations through the readout of most current ongoing/planned Phase I/II trials.

## Disclosures Appendix

### Analyst Certification

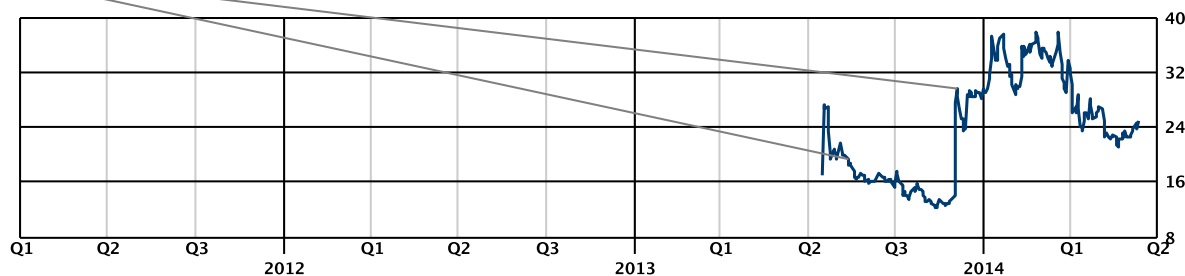
I, Howard Liang, Ph.D., certify that the views expressed in this report accurately reflect my views and that no part of my compensation was, is, or will be directly related to the specific recommendation or views contained in this report.

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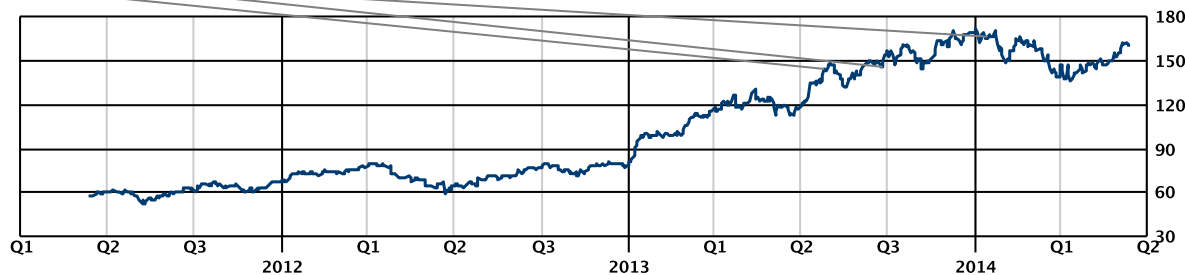
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**Rating and Price Target History for: OncoMed Pharmaceuticals, Inc. (OMED) as of 06-12-2014**
08/12/13  
I:OP:\$2712/04/13  
OP:\$37

On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

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**Rating and Price Target History for: Celgene, Inc. (CELG) as of 06-12-2014**
07/26/13  
OP:\$16509/25/13  
OP:\$17701/14/14  
OP:\$197

Leerink Swann initiated coverage of CELG with an Outperform rating on February 7, 2003. On June 11, 2013, Leerink Swann began a transition to specific price targets for the stocks under its coverage, replacing valuation ranges.

OP=Outperform MP=Market Perform UP=Underperform D=Drop Coverage I=Initiate SC=Suspend Coverage

Created by BlueMatrix

Distribution of Ratings/Investment Banking Services (IB) as of 03/31/14				
Rating	Count	Percent	IB Serv./Past 12 Mos.	
			Count	Percent
BUY [OP]	131	68.23	46	35.11
HOLD [MP]	61	31.77	3	4.92
SELL [UP]	0	0.00	0	0.00

## Explanation of Ratings

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

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

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

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

## Important Disclosures

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**In the past 12 months, the Firm has received compensation for providing investment banking services to OncoMed Pharmaceuticals, Inc. .**

**Leerink Partners LLC makes a market in OncoMed Pharmaceuticals, Inc. and Celgene, Inc.**

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

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