March 9, 2015

OUTPERFORM

Reason for report:

FLASH NOTE

Joseph P. Schwartz
(617) 918-4575
Joseph.Schwartz@Leerink.com

Paul Matteis
(617) 918-4585
Paul.Matteis@Leerink.com

LEERINK

ZAFGEN, INC.

Full Ph. II HIAO Dataset at ENDO '15 Further De-risks Late-Stage Development

• **Bottom Line:** After reporting positive top-line Ph. II beloranib data in Hypothalamic Injury-Associated Obesity (HIAO) back in Jan. '15, ZFGN presented the full dataset at the ENDO '15 meeting over the weekend in the form of a late-breaking poster. Recall, the top-line data were constituted of the statistically significant (p=0.01) benefit in mean weight loss of 3.4 kg vs. 0.3 kg on beloranib (n=8) vs. pbo (n=6) treatment arms at 4-weeks, which in the follow-on open-label portion of the study where all 14 pts received beloranib until 8-weeks showed mean weight loss of 6.2 kg vs. 3.2 kg on beloranib (4 wks) -- > beloranib (4 wks) vs. pbo (4 wks) -- > beloranib (4 wks). This effect seen in the pbo arm (not previously disclosed) following crossover on beloranib is further validation of the drug's MetAP2 inhibition translating into significant weight loss. Reiterate OP with a PT of $42.

• **Cardiometabolic and inflammation biomarkers of efficacy were all significantly improved (p-value<0.05)** in the beloranib (4 wks) -- > beloranib (4 wks) vs. pbo (4 wks) -- > beloranib (4 wks) [change from baseline in i) total cholesterol: -20.6 vs. 14.6 mg/dL], ii) LDL: -18.6 vs. -12.4 mg/dL, iii) HDL: +3.8 vs. +5.6 mg/dL, iv) triglycerides: -41.2 vs. -31.5 mg/dL, and v) hs-CRP (measures inflammation) at 4 wks: -13.7 vs. -4.7 mg/L & at 8 wks: -9.6 vs. -12.3 mg/L. In our view, this coupled with weight loss data further de-risks beloranib's late-stage development, mainly: a) Ph. III pivotal trial in Prader-Willi syndrome (PWS), which is expected to report data by YE15, and b) ZFGN's ongoing regulatory discussions with FDA/EMA on the design of first-of-its-kind pivotal program in HIAO. Cardiometabolic parameters in particular bode well for the Ph. III proof-of-concept study in obese pts with Type II Diabetes expected to read out top-line data in 4Q15.

• **On the safety front, no severe/serious AEs were reported with 2/8 pts (25%) on beloranib arm experiencing mild & transient dizziness and headaches vs. pbo arm reporting only headache in 2/6 pts (33%).** In line with previously known effects on the CNS, this may be something to manage, although in serious orphan diseases like PWS and HIAO it shouldn't change meaningfully the risk/benefit profile or how many pts may be eligible candidates for the drug, in our view.

• **No change in perceived hunger (sign of damaged hypothalamus) observed in 8-question Visual Analog Score (8-Q VAS), while stat. sig. reduction in prospective food intake observed in beloranib vs. pbo (-38% vs. -55%).** This differentiation of "*sense of hunger"* from "*drive to eat"* enables the investigators to conclude beloranib's mechanistic effect on extrahypothalamic pathways. Mgmt. remains committed to further rationalizing this effect of beloranib on hyperphagia causing weight loss (independent from a fully functional hypothalamus) with additional preclinical & translational work.

Key Stats:	**(OTC Un:ZFGN)**
S&P 600 Health Care Index:	**1,569.15**
Price:	**$38.75**
52 Week High:	$43.03
52 Week Low:	$16.01
Shares Outstanding (mil):	24.2
Market Capitalization (mil):	$937.8

VALUATION

We derive a ~$42 per share value for ZFGN using a 12% discount rate and a 2% terminal growth rate, representing an ~$860MM market capitalization. Our price target assumes an 80% and 60% probability of beloranib approval in PWS and HIAO, respectively, which leads to our peak net sales estimates of ~$560MM and ~$270MM in each indication. We only model ~$140MM in peak sales in severe obesity, which we believe holds the potential to be very conservative if/when ZFGN generates pivotal beloranib data in orphan indications.

RISKS TO VALUATION

Risks to our valuation include disappointing clinical data, regulatory setbacks, dilution risk from an additional equity offering, and commercial shortfalls. Because ZFGN has only one late-stage product, the occurrence of any of these could impact the stock significantly.

Disclosures Appendix

Analyst Certification

I, Joseph P. Schwartz, 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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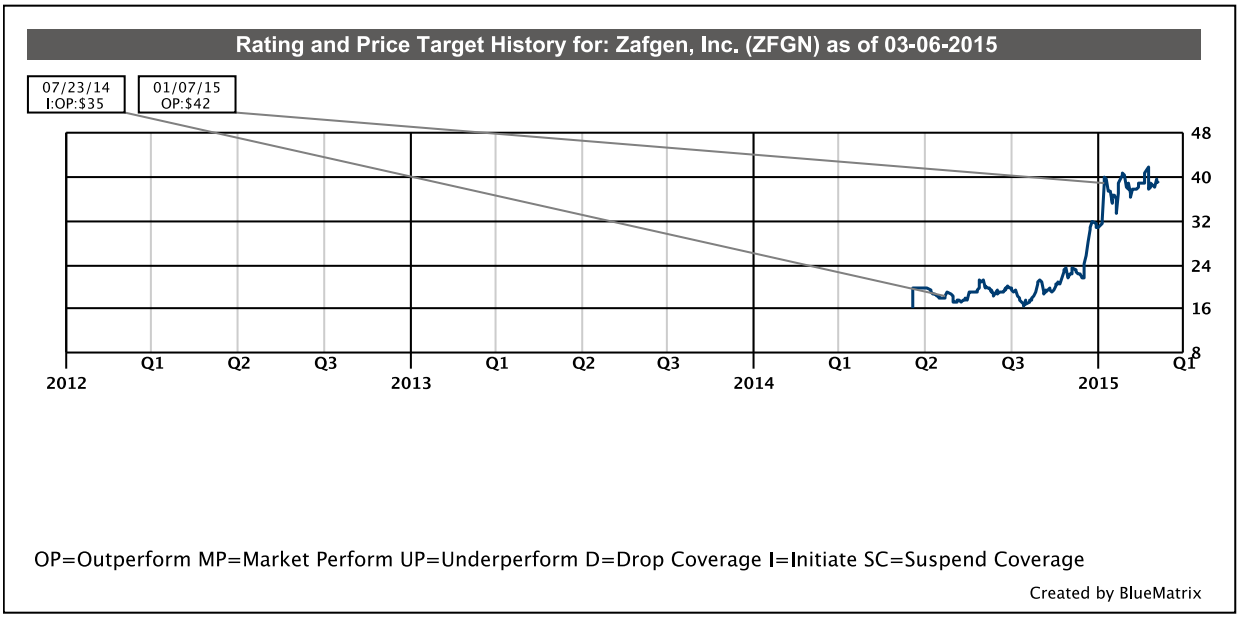

Distribution of Ratings/Investment Banking Services (IB) as of 12/31/14				
			IB Serv./Past 12 Mos.	
Rating	Count	Percent	Count	Percent
BUY [OP]	150	70.00	61	41.00
HOLD [MP]	64	30.00	0	0.00
SELL [UP]	0	0.00	0	0.00

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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Leerink Partners LLC makes a market in Zafgen, Inc.

Leerink Partners LLC has acted as the manager for a public offering of Zafgen, 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
	Michael Schmidt, Ph.D.	(617) 918-4588	michael.schmidt@leerink.com
	Gena Wang, Ph.D., CFA	(212) 277-6073	gena.wang@leerink.com
	Paul Matteis	(617) 918-4585	paul.matteis@leerink.com
	Jonathan Chang, Ph.D.	(617) 918-4015	jonathan.chang@leerink.com
	Richard Goss	(617) 918-4059	richard.goss@leerink.com
Life Science Tools	**Dan Leonard**	(212) 277-6116	dan.leonard@leerink.com
and Diagnostics	Justin Bowers, CFA	(212) 277-6066	justin.bowers@leerink.com
	Kevin C. Chen	(212) 277-6045	kevin.chen@leerink.com
Pharmaceuticals/Major	**Seamus Fernandez**	(617) 918-4011	seamus.fernandez@leerink.com
	Aneesh Kapur	(617) 918-4576	aneesh.kapur@leerink.com
Specialty Pharmaceuticals	**Jason M. Gerberry, JD**	(617) 918-4549	jason.gerberry@leerink.com
	Derek C. Archila	(617) 918-4851	derek.archila@leerink.com
Medical Devices, Cardiology	**Danielle Antalffy**	(212) 277-6044	danielle.antalffy@leerink.com
	Puneet Souda	(212) 277-6091	puneet.souda@leerink.com
& Orthopedics	**Richard Newitter**	(212) 277-6088	richard.newitter@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	**David Larsen, CFA**	(617) 918-4502	david.larsen@leerink.com
& Distribution	Christopher Abbott	(617) 918-4010	chris.abbott@leerink.com
Digital Health	**Steven Wardell**	(617) 918-4097	steven.wardell@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
Editorial	Cristina Diaz-Dickson	(617) 918-4548	cristina.diaz-dickson@leerink.com
Research Associate	Carmen Augustine	(212) 277-6012	carmen.augustine@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