Zafgen, Inc. (ZFGN)

Increasing Price Target to Reflect Positive HIAO Data and Reinforced Confidence in Positive Phase 3 in PWS

MARKET DATA

Price	$38.50
52-Week Range:	$16.01 - $32.25
Shares Out. (M):	22.7
Market Cap ($M):	$874.0
Average Daily Vol. (000):	105.0
Cash (M):	$127
Cash/Share:	$5.59
Enterprise Value (M):	$852
LT Debt (M):	$0

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2013A	2014E	2015E
Revenue ($M)	1Q	$0.0	$0.3A	--
	2Q	$0.0	$0.0A	--
	3Q	$0.0	$0.0A	--
	4Q	$0.0	$0.0	--
	FY	**$0.0**	**$0.3**	**$0.0**
EPS	1Q	($4.94)	($5.82)A	--
	2Q	--	($2.96)A	--
	3Q	--	($0.65)A	--
	4Q	--	($0.86)	--
	FY	**($19.53)**	**($10.28)**	**($2.13)**

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

MARKET OUTPERFORM | Price: $38.50 | Target Price: $50.00

INVESTMENT HIGHLIGHTS

Positive Phase 2 results in HIAO patients reinforce our confidence broadly for beloranib severe obesity indications, including PWS; reiterate our Market Outperform rating and increasing our price target on Zafgen from $31 to $50. This morning, Zafgen announced positive results from a Phase 2 proof-of-concept trial evaluating beloranib in patients with Hypothalamic Injury-Associated Obesity (HIAO, or "acquired PWS"). These results demonstrated significant weight loss efficacy for beloranib in this patient population with a high unmet medical need and, in our view, support its advancement into a pivotal program. Furthermore, we believe these data support the differentiated efficacy of beloranib and reinforce our confidence in the ongoing Phase 3 trial in patients with Prader-Willi Syndrome and Phase 2b trial in patients with severe obesity and type 2 diabetes (results from both trials are expected by YE 2015). Our $50 price target is derived though a sum-of-the-parts NPV analysis of beloranib in PWS, and in hypothalamic injury-associated obesity.

Phase 2 results support consistent weight loss efficacy across severe obese patient populations. The Phase 2 ZAF-221 trial (NCT02063295) enrolled 14 patients with HIAO who received treatment with beloranib or placebo for four weeks. The results demonstrated statistically significant weight loss with beloranib vs. placebo ($p = 0.01$) at four weeks with beloranib treated patients losing on average 3.4kg at, vs. 0.3kg with placebo. Weight loss efficacy with beloranib increased over an additional, optional four-week, open-label extension reaching 6.2kg.

Looking to details on secondary endpoints, including hunger assessments, at an upcoming medical conference, as well as input from the FDA on the development path forward. Based on our discussion with management, we anticipate that results from this trial will be submitted for presentation at a medical conference in 1H15 (possibly in 1Q15). In addition to weight loss efficacy, we look to details on further benefits including potential improvements in cardiovascular risk parameters and hunger-related behaviors. ZFGN plans to discuss next steps with the FDA in coming months for development in this indication, likely as a line extension strategy to a PWS label.

Increasing price target to reflect reinforced confidence in beloranib as a differentiated treatment option for patients with limited/no effective treatment options. We increased our probability of success for beloranib in the HIAO population from 60% to 75% and projected peak penetration from 20% to 25%. We also increased the probability of success in the PWS population from 75% to 80%. We increased the contribution margin in our NPV analysis from 40% to 45% to reflect the specialty nature of sales and marketing effort for an orphan drug such as beloranib. Our valuation now discounts through YE 2015, vs. prior YE 2014.

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PHASE 2 TRIAL EVALUATING BELORANIB IN HIAO PATIENTS

The Phase 2a ZAF-221 trial (NCT02063295) was a proof-of-concept study evaluating beloranib in patients with Hypothalamic Injury-Associated Obesity (HIAO). The trial was a randomized, double-blind, placebo controlled study that enrolled 14 obese patients (nine women and five men) who were confirmed by magnetic resonance imaging (MRI) to have had hypothalamic injury. Patients were randomized to receive beloranib (1.8mg) twice weekly or placebo for a four-week, double-blind treatment period, followed by an optional four-week, open-label extension. The primary endpoint was change in body weight, with additional endpoints including metabolic risk markers (i.e., cholesterol, triglycerides, CRP), assessments of hunger, and quality of life.

Treatment with beloranib resulted in mean weight loss of 3.4kg after four weeks, significantly greater than the 0.3kg mean weight loss in patients treated with placebo for four weeks ($p = 0.01$). At the end of the open-label extension, weight loss in beloranib treated patients increased to 6.2kg. In addition, the company stated that improvements were seen in lipids and inflammation (as measured by CRP). We look to additional details on the results from this trial at a medical meeting in 1H15, including beloranib's effects on hunger. Management intends to discuss the next development steps with the FDA and EMA in 2015.

Mechanistic and clinical rationale for beloranib in HIAO

Beloranib is a first-in-class MetAP2 inhibitor which has been shown to act through the liver and adipose tissue to balance lipid metabolism and, notably, reduce hunger. In five Phase 1/2 trials conducted by Zafgen, beloranib demonstrated consistent weight loss, including in patients with PWS. In addition, the Phase 2a trial in PWS showed an improvement in hyperphagia (severe hunger) in addition to weight loss. In our view, these results provide strong rationale that beloranib would also show benefit in HIAO. Both conditions are caused by underlying pathology in the hypothalamus and the similarity of clinical symptoms presented.

Although etiology in HIAO differs from PWS (Prader-Willi Syndrome), which is caused by a genetic mutation in the 15th chromosome, both conditions involve damage and/or impairment of the hypothalamus. HIAO is caused by damage to the hypothalamus, for example, following surgical removal of craniopharyngioma, a benign tumor in the vicinity of the hypothalamus. Such damage often results in loss of appetite control and reduced metabolic rate which leads to obesity. Importantly, both HIAO and PWS patients exhibit the same clinical symptoms of a slow metabolic rate, hyperphagia, and obesity. Having now established proof-of-concept in HIAO, we are encouraged that Zafgen may continue to leverage beloranib in several indications including severe obesity. A Phase 2b trial evaluating the drug candidate in patients with severe obesity and Type 2 diabetes (NCT02324491) was initiated December 2014 and results are expected by YE 2015. We note that the use of beloranib in this setting, and other severe obesity indications beyond PWS and HIAO, represent upside to our current valuation assumptions.

Company Description

Zafgen is a biopharmaceutical company focused on addressing the unmet need of severely obese patients and related orphan indications. The company's lead development candidate is beloranib, a first-in-class MetAP2 inhibitor. Initial development of beloranib is targeting obesity and hyperphagia, or insatiable life-threatening hunger and hunger-related behaviors, in patients with Prader-Willi Syndrome (PWS) and craniopharyngioma-associated obesity. Additional indications for beloranib, and second generation MetAP2 inhibitors, include severe obesity in the general population, NASH, and Type 2 diabetes. The company is lead by an experienced management team with proven success in the cardiovascular and metabolic disease arenas.

Zafgen completed its IPO in June 2014 and raised net proceeds of ~$103MM. We believe the IPO proceeds provide sufficient cash to fund operations into 2017, which include full clinical development of beloranib in Prader-Willi Syndrome.

Investment Risks

Clinical risk. We note that positive results from early trials cannot always be replicated and that the drug may fail in later trials. We note that the Phase 2a proof-of-concept trial was conducted in a small number of patients (n=14), although we believe the likelihood of replicating these positive results in a Phase 3 trial is high. Zafgen may not be successful in the full development and launch of its product candidate, beloranib. There may be dosing, efficacy, or safety issues related to product candidates undergoing clinical trials that could preclude continued development. In addition, there may be manufacturing issues including challenges with the scale-up to commercial quantities. Any of these issues could pose a risk to success.

Regulatory risk. The company’s potential regulatory filing for its NDA may not receive approval from the FDA or ex-U.S. agencies. The FDA may request further studies, in which case the approval pathway will likely take longer and cost significantly more. Zafgen relies on third parties to conduct future clinical trials of beloranib and there is risk that they may not carry out their contractual duties or meet deadlines, either of which would result in delays and adverse consequences to the business.

Market risk. Market estimates of PWS patients, or patients eligible for beloranib treatment, may be overestimated. This would impact the ability to reach revenue and profitability projections. The company must retain its intellectual property rights. Other companies may file patent applications or may receive patents that claim the same methods or formulations. This competition would affect operations and potential business prospects.

Financial risk. Zafgen has funded operations to date through proceeds from sales of redeemable convertible preferred stock and convertible debt. Due to no incoming revenue as of yet, the company has incurred losses each year since inception due to research and development expenses. These expenses are expected to continue to incur in the near future. We anticipate that Zafgen will likely need to raise additional funds in the next 12 months to continue future operations. If there are any issues commercializing its product candidates and achieving sales revenue, the company may not reach profitability, which may jeopardize the business. Additionally, Zafgen shares are subject to market volatility risk.

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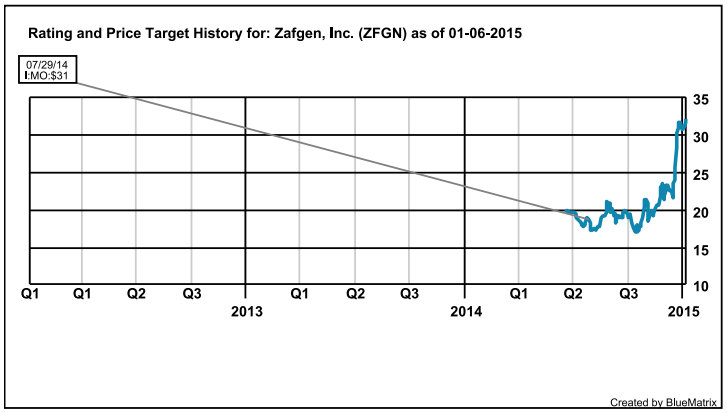
MARKET OUTPERFORM	Buy	295	*65.41%*	Buy	295	*65.41%*	102	*34.58%*
MARKET PERFORM	Hold	150	*33.26%*	Hold	150	*33.26%*	17	*11.33%*
MARKET UNDERPERFORM	Sell	3	*0.67%*	Sell	3	*0.67%*	0	*0%*
COVERAGE IN TRANSITION		1	*0.22%*		1	*0.22%*	0	*0%*
TOTAL:		451	*100%*		451	*100%*	121	*26.83%*

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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