

Equity Research

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Price: \$32.17 (01/6/2015)

Price Target: \$45.00

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: ZFGN
Market Cap (MM)	\$730.5

Quick Take: Company Update

Beloranib's Phase II In HIAO Successful

The Cowen Insight

This morning ZFGN announced positive results from ZAF-221, a Ph. II trial of beloranib in patients with hypothalamic injury associated obesity (HIAO). Beloranib was well tolerated and achieved a mean weight reduction over 4 weeks of 3.4 kg vs. 0.3 kg with placebo ($p=0.01$). We continue to think that Zafgen is undervalued based on beloranib's potential in HIAO and Prader-Willi.

The News: This morning, Zafgen announced positive results from beloranib's Phase II trial (ZAF-221) in patients with hypothalamic injury associated obesity (HIAO). Beloranib is a MetAP2 inhibitor that has demonstrated efficacy in weight loss and hunger reduction in prior trials in obesity associated indications. ZAF-221 met its primary endpoint as patients treated with 1.8 mg beloranib achieved a mean weight reduction after 4 weeks of 3.4 kg versus a 0.3 kg reduction in patients treated with placebo ($p=0.01$). Patients who participated in the optional four week open-label extension had a mean weight reduction of 6.2 kg over the eight week treatment period. Patients treated with beloranib also benefited from improvements in cardiovascular disease risk factors including lipids, and inflammation as measured by C-reactive protein. Beloranib was well tolerated and safe with no serious or severe AEs reported in the trial. ZAF-221 enrolled and randomized 14 obese patients (nine women and five men) with MRI confirmed HIAO and BMI of greater or equal to 30 kg/m² and less than or equal to 60 kg/m² to receive twice-weekly subQ injections of 1.8 mg beloranib or placebo over a four week study period.

Our Take: We view the positive results from the Phase II ZAF-221 study in HIAO as impressive. The mean weight reduction of 3.4 kg and 6.2 kg over four and eight weeks is consistent with results observed in beloranib's previous Phase II trial in obese patients (12-week treatment with 1.2 mg beloranib led to mean weight reduction of 6.9 kg ($p<0.0001$)). Just as important, we think this morning's data provides further evidence of beloranib's ability to reduce weight in individuals with hypothalamic dysfunction. As hypothalamic dysfunction is thought to also cause the obesity and hyperphagia associated with Prader-Willi, this morning's data further de-risks beloranib's Phase III in Prader-Willi (initial six-month data in Q4:15), in our opinion. Our model projects that beloranib will achieve 2025 world-wide sales of \$925MM, of which \$445MM is in HIAO, and \$480MM is in Prader-Willi. Today's data give us increased confidence in these estimates.

Upcoming Milestones: Zafgen is planning to initiate a Ph. III trial of beloranib in PWS in the E.U. by H1:2015. Zafgen anticipates IND filings for ZGN-839 in type II diabetes, NASH, and abdominal obesity in H1:15. Zafgen expects to provide interim six-month Phase IIb data from beloranib in severe obesity in Q4:15. Zafgen expects

to announce initial six-month data from its U.S. Phase III trial of beloranib in PWS by Q4:15.

Our Investment Thesis: Prader-Willi syndrome and hypothalamic injury associated obesity (HIAO) are orphan disorders that each afflict approximately 20K patients in the U.S. and E.U. We estimate that beloranib could address a \$1B+ opportunity in these two conditions. Behind beloranib, Zafgen is developing an orally active second-generation MetAP2 inhibitor, ZGN-839, in Nonalcoholic Steatohepatitis (NASH) and type 2 diabetes. Our DCF analysis suggests that Zafgen is undervalued based on beloranib's potential in Prader-Willi and craniopharyngioma-associated obesity alone, with no contribution from other indications or pipeline programs.

Valuation Methodology And Risks

Valuation Methodology

Biotechnology:

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

Risks To The Price Target

Zafgen is developing candidates for the treatment of orphan disorders, obesity, and metabolic conditions. The majority of Zafgen's market capitalization is dependent upon the success of lead candidate beloranib. Beloranib's value could be adversely impacted should its clinical trials fail, should the regulatory agencies deny approval, or should its commercial opportunity not materialize as we project. In fact, all of Zafgen's drug candidates face clinical and regulatory risk. With the future development path depending on the evolution of clinical data, future revenue forecasts are uncertain. The commercial outlook for Zafgen's candidates could additionally be altered by safety/efficacy findings, emerging competition, alterations in the medical treatment paradigm, or changes in the pricing environment. Some of Zafgen's projected market exclusivity depends on patents, which are subject to challenge by generic drugmakers.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
ZFGN	Zafgen

Analyst Certification

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Cowen and Company Rating System effective May 25, 2013

Outperform (1): The stock is expected to achieve a total positive return of at least 15% over the next 12 months

Market Perform (2): The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform over the next 12 months

Underperform (3): Stock is expected to achieve a total negative return of at least 10% over the next 12 months

Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

Outperform (1): Stock expected to outperform the S&P 500

Neutral (2): Stock expected to perform in line with the S&P 500

Underperform (3): Stock expected to underperform the S&P 500

Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

Cowen Securities, formerly known as Dahlgren Rose & Company, Rating System until May 25, 2013

Buy – The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market return

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Hold – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

Cowen And Company Rating Definitions

Distribution of Ratings/Investment Banking Services (IB) as of 12/31/14

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	461	60.50%	109	23.64%
Hold (b)	288	37.80%	14	4.86%
Sell (c)	13	1.71%	0	0.00%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

Note: "Buy", "Hold" and "Sell" are not terms that Cowen and Company, LLC uses in its ratings system and should not be construed as investment options. Rather, these ratings terms are used illustratively to comply with FINRA and NYSE regulations.

Zafgen Rating History as of 01/06/2015

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Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | \$xx = Price Target | NA = Not Available | S=Suspended

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