


RBC Capital Markets

RBC Capital Markets, LLC
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Zafgen, Inc.

Full HIAO data impress; the sleeper obesity name with 3 independent shots on goal

ZFGN presented the impressive full dataset of the previously released top-line ZAF-221 Phase II data of beloranib in HIAO.

In early January, ZFGN announced top-line data from beloranib's ZAF-221 Phase II trial in Hypothalamic Injury Associated Obesity (HIAO). The company provided the full ZAF-221 results in a poster presentation this weekend at the ENDO conference in San Diego.

Study information: HIAO is a rare disease in which patients have lost the ability to regulate metabolism and food intake due to injuries to the hypothalamus resulting from prior CNS surgeries. ZAF-221 is a randomized, double-blind, placebo-controlled study involving 14 HIAO patients (8 drug/6 placebo) receiving twice-weekly subcutaneous injections of 1.8 mg beloranib or placebo over a course of 4 weeks with an optional 4-week extension. The study met its primary endpoints of weight loss and safety, and no serious or severe AE were observed. Efficacy analysis was on 12 patients (8 beloranib/4 placebo) since one placebo-randomized patient discontinued due to a suspected allergic reaction and another placebo-randomized patient was excluded from efficacy analysis due to a dosing error.

Beloranib induced rapid and impressive weight loss. Following 4 weeks of beloranib treatment, patients lost an average of -3.40 ± 0.6 kg (7.5lbs) of body weight vs. -0.25 ± 0.8 kg (0.5lbs) for placebo ($p=0.01$). Following an additional 4 weeks of open-label extension, patients initially randomized to beloranib lost a total of -6.15 ± 0.9 kg (13.5lbs) of body weight vs. -3.0 ± 1.3 kg (6.6lbs) (for patients originally in the placebo-delayed group). This rapid weight loss, which showed no signs of slowing down at the 8-week timepoint, was achieved without the aid of increased exercise or dietary changes, underscoring the impressive efficacy of beloranib (see page 2 for the weight loss graph).

Clean safety profile. Mild and transient dizziness, headache, and nasopharyngitis (2 patients [25.0%]) were the only AEs that occurred in more than one patient treated with beloranib. By comparison, headache was reported in 2 placebo patients (33%), and nasopharyngitis occurred in one placebo patient (16.7%). There were only 5 instances of moderate AEs with beloranib, 2 for placebo, while there were no reports of severe or serious AE. Finally, no beloranib patients withdrew due to an AE.

Improvements in lipids, CRP. Patients receiving beloranib for 8 weeks exhibited a mean 18.6 mg/dL reduction from baseline in measured LDL levels vs. a 12.4 mg/dL reduction for the group receiving 4 weeks of beloranib treatment following 4 weeks of placebo ($p<0.05$). Beloranib also induced a mean 41.2 mg/dL reduction from baseline in triglyceride levels vs. a 31.5 mg/dL reduction for the placebo-delayed group ($p<0.05$).

**Outperform
Speculative Risk**

NASDAQ: ZFGN

Price: USD 38.75

All values in USD unless otherwise noted.

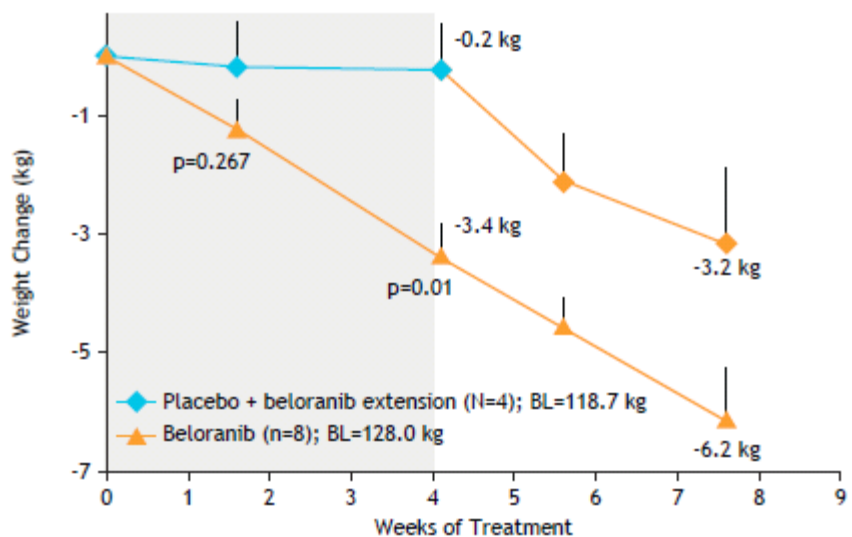
Furthermore, levels of C-Reactive Protein (CRP) decreased by a mean of 13.7 mg/L from baseline after 4 weeks of beloranib treatment vs. a mean 4.7 mg/L decrease after 4 weeks of placebo ($p=0.009$). These data indicate that beloranib's weight loss effect in HIAO patients is associated with concomitant reductions in levels of lipids and inflammatory biomarkers linked to increased risk of cardiovascular disease.

What's next for ZFGN: **1)** Submit IND for oral ZGN-839 program in NASH/T2DM, mid 2015; **2)** Initiate second PWS trial (ZAF-312) in EU, mid 2015; **3)** 6-month Ph III best PWS readout, YE15; **4)** Interim Ph II ZAF-203 data in severe obesity, YE15; **5)** NDA submission for beloranib in PWS, 2016; and **6)** 12-month data from ZAF-312 PWS trial, YE16.

ZFGN's beloranib: A very impressive injectable drug for obesity... Beloranib acts via a novel mechanism of action (MOA) to lead to rapid and impressive weight loss in the obese patients it has been tested on in early-stage Phase I and II trials. Using a different MOA than the ones used by the weight-loss drugs currently on the market, this methionine aminopeptidase 2 (MetAP2) inhibitor leads to significant weight loss (up to 10% of body weight) in just 12 weeks. Two factors make this efficacy even more impressive: 1) it was achieved without the benefit of any diet or exercise; and 2) this weight loss did not seem to plateau after 12 weeks of treatment, suggesting that even more weight loss could be achieved with longer treatment.

...but it will not get to the market for obesity first: However, and despite this impressive efficacy, Zafgen has decided to not go with obesity as its first indication for beloranib, but rather to test it in rare diseases instead. If successful, this strategy may get the drug to the market faster, in addition to other benefits, including premium pricing.

Exhibit 1: Mean Change in Body Weight over Time



Source: Company presentation



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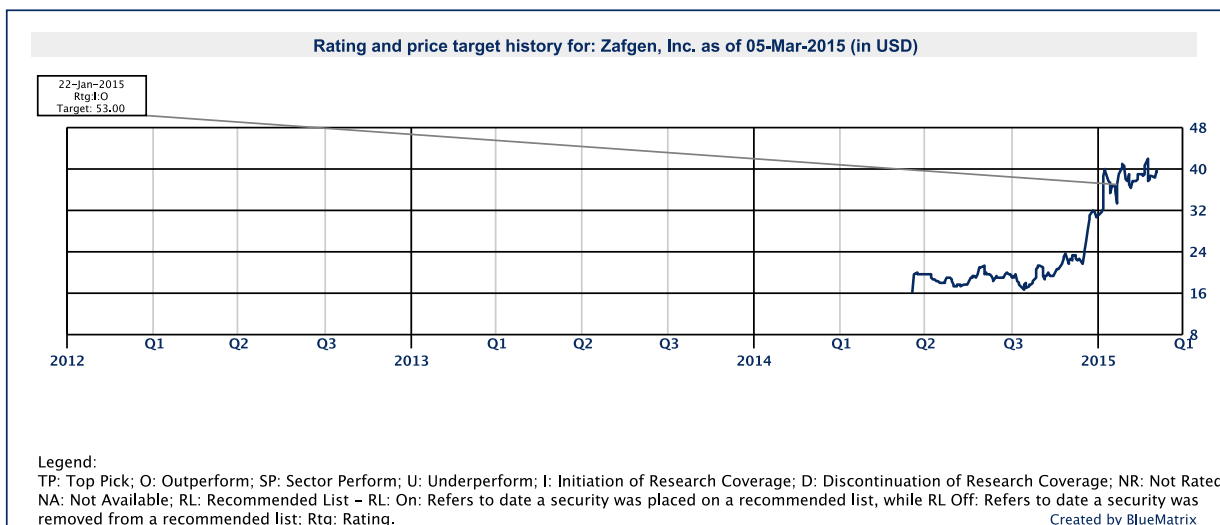
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			Count	Percent
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