COWEN
AND COMPANY

Biotechnology

Zafgen

Equity Research

Initiating Coverage

July 14, 2014

Price: $18.63 (07/10/2014)
Price Target: $45.00

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: ZFGN
52-Week Range:	$21.01 - 17.87
Market Cap (MM):	$406.3
Net Debt (MM):	$(35.5)
Cash/Share:	NA
Dil. Shares Out (MM):	22.7
Enterprise Value (MM):	$479.5
ROIC:	NA
ROE (LTM):	NA
BV/Share:	$(99.95)
Dividend:	NA

FY (Dec)	2014E	2015E	2016E
Earnings Per Share			
Q1	$(0.98)A	-	-
Q2	$(0.43)	-	-
Q3	$(0.84)	-	-
Q4	$(0.48)	-	-
Year	$(2.50)	$(2.45)	$(2.75)
P/E	NM	NM	NM
Revenue (MM)			
Year	$0.0	$0.0	$0.0
EV/S	-	-	-

Initiation: An Insatiable Hunger For Zafgen

The Cowen Insight

Zafgen's lead candidate beloranib is in development for hyperphagia and obesity. We and our consultants think it is quite promising in the orphan indications Prader-Willi Syndrome and craniopharyngioma-associated obesity. We estimate that beloranib could address a $1.5B+ opportunity in these two conditions. Today we are initiating coverage with an Outperform rating and a $45 price target.

Beloranib To Begin Phase III In Prader-Willi During H2.

Beloranib is a novel small molecule inhibitor of methionine aminopeptidase 2 (MetAP2) that is in development for the treatment of hyperphagia (insatiable appetite) and obesity in Prader-Willi syndrome, craniopharyngioma-associated obesity, and severe obesity in the general population. Zafgen has completed five clinical trials in over 200 subjects including obese volunteers and Prader-Willi Syndrome patients. In these trials beloranib has reduced fat mass and controlled hyperphagia while maintaining an acceptable tolerability and safety profile. Our consultants find the >50% decrease in hyperphagia produced in Prader-Willi patients particularly striking, as beloranib is the first agent shown to produce a reduction in food seeking behaviors in these patients, a key area of unmet need. Beloranib will enter a Phase III trial in Prader-Willi syndrome during H2:14, with initial data possible in Q4:2015. A Phase IIa trial in craniopharygioma-associated obesity is ongoing, with data expected Q1:15.

Beloranib Could Be A $1B+ Opportunity In The Orphan Disorders Alone.

Prader-Willi syndrome and craniopharyngioma-associated obesity are orphan disorders that each afflict approximately 20K patients in the U.S. and EU. Our consultants think that beloranib's Phase II data in PWS is "impressive," and they are hopeful that it will be successfully developed. They find the impact of beloranib's 1.8mg dose on hyperphagia particularly meaningful and think that should beloranib reduce hyperphagia by 50% in the real world, it would become standard of care, appropriate for most patients. We estimate that beloranib could address a $1.5B+ opportunity in these two conditions.

Pipeline Programs Address Large Markets, Too.

Zafgen will initiate a Phase IIb trial of beloranib in general obesity, with data possible in Q4:2015. In a Phase IIa trial beloranib produced placebo-adjusted weight loss of up to 10.3% after 12 weeks of treatment. This suggests that beloranib has the potential to be as effective as surgical procedures. Zafgen is developing an orally active second-generation MetAP2 inhibitor, ZGN-839. ZGN-839 has shown early efficacy in preclinical models of Nonalcoholic Steatohepatitis (NASH) and type 2 diabetes. Zafgen plans to submit an IND for ZGN-839 in H1:15.

We Think Zafgen Is Undervalued Based On The Orphan Indications.

Our DCF analysis suggests that Zafgen is undervalued based on beloranib's potential in Prader-Willi and craniopharyngioma-associated obesity alone. Our DCF-based price target is $45.

Please see addendum of this report for important disclosures.

At A Glance

Our Investment Thesis

Zafgen's lead asset beloranib is in development for the treatment of hyperphagia (insatiable appetite) and obesity in Prader-Willi syndrome, craniopharyngioma-associated obesity, and severe obesity in the general population. Zafgen has completed five clinical trials in over 200 subjects including obese volunteers and Prader-Willi Syndrome patients. In these trials beloranib has reduced fat mass and controlled hyperphagia while maintaining an acceptable tolerability and safety profile. Our consultants find the >50% decrease in hyperphagia produced in PWS patients particularly striking, as beloranib is the first agent shown to produce a reduction in food seeking behavior. Beloranib will enter a Phase III trial in Prader-Willi syndrome during H2:14, with initial data possible in Q4:2015. Our DCF suggests that Zafgen is undervalued based on beloranib's potential in Prader-Willi and craniopharyngioma alone, with no contribution from other indications or pipeline programs.

Forthcoming Catalysts

- Initiate Phase III trial of Beloranib in Prader-Willi, H2:14
- Initiate Phase IIb trial of Beloranib in severe obesity, H2:14
- Initial data from Ph. IIa of Beloranib in craniopharyngioma, Q1:15
- Initial data from Ph. III trial of Beloranib in Prader-Willi, Q4:15

Base Case Assumptions

- Beloranib is successfully developed for Prader-Willi and craniopharyngioma, achieving $1.0B in sales by 2026.
- Beloranib is not developed for any other indications.
- The rest of Zafgen's pipeline does not contribute significant value.

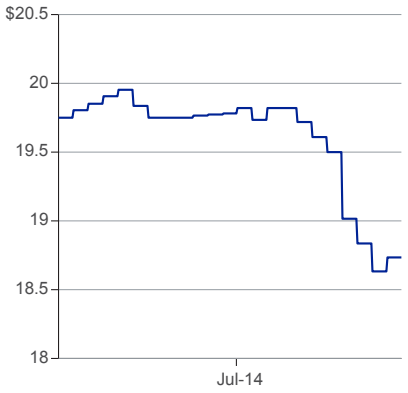
Upside Scenario

- Beloranib is successfully developed for Prader-Willi and craniopharyngioma, achieving >$1.0B in sales by 2026.
- Beloranib is also successfully developed for other indications.
- ZGN-839 is successfully developed for NASH and/or type 2 diabetes
- Another pipeline candidate contributes significant value.

Downside Scenario

- Beloranib is not successfully developed for Prader-Willi and/or craniopharyngioma.
- Beloranib does not achieve $1.0B in sales by 2026.
- The rest of Zafgen's pipeline does not contribute much value.

Price Performance



Source: Bloomberg

Company Description

Zafgen is a biopharmaceutical company dedicated to improving the health and well-being of patients affected by obesity. Zafgen's beloranib is a novel small molecule inhibitor of methionine aminopeptidase 2 (MetAP2). In addition to a Phase III trial of beloranib in Prader-Willi, Zafgen will also initiate a Phase IIb trial in general obesity during H2:14, with data possible in Q4:15. A Phase IIa trial in craniopharygioma-associated obesity is ongoing, with data expected during Q1:15. Prader-Willi syndrome and craniopharyngioma-associated obesity are orphan disorders that each afflict approximately 20K patients in the U.S. and EU. We estimate that beloranib could address a $1.5B+ opportunity in these two conditions. Behind beloranib, Zafgen is developing an orally active MetAP2 inhibitor, ZGN-839. ZGN-839 has shown early efficacy in preclinical models of Nonalcoholic Steatohepatitis (NASH) and type 2 diabetes. Zafgen plans to submit an IND for ZGN-839 in H1:15.

Analyst Top Picks

	Ticker	Price (07/10/2014)	Price Target	Rating
BioMarin Pharmaceutical	BMRN	$59.06	$95.00	Outperform
Gilead Sciences	GILD	$88.94	$95.00	Outperform
Portola Pharmaceuticals	PTLA	$25.62	$45.00	Outperform

A Novel Mechanism To Treat Disease-Associated Obesities

Investment Thesis

Zafgen is a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by obesity. Zafgen's lead asset, beloranib, is a novel small molecule inhibitor of methionine aminopeptidase 2 (MetAP2) that is in development for the treatment of hyperphagia (insatiable appetite) and obesity in Prader-Willi Syndrome, craniopharyngioma-associated obesity, and severe obesity in the general population. Zafgen has completed five clinical trials in over 200 subjects including obese volunteers and Prader-Willi Syndrome patients. In these trials Beloranib has reduced fat mass and controlled hyperphagia while maintaining an acceptable tolerability and safety profile. Our consultants find the >50% decrease in hyperphagia produced in Prader-Willi patients particularly striking, as beloranib is the first agent shown to produce a reduction in food seeking behaviors in these patients, a key area of unmet need. Beloranib will enter a Phase III trial in Prader-Willi Syndrome during H2:14, with initial data possible in Q4:2015. Zafgen will also initiate a Phase IIb trial in general obesity, with data possible in Q4:2015. A Phase IIa trial in craniopharyngioma-associated obesity is ongoing, with data expected during Q1:2015. Prader-Willi Syndrome and craniopharyngioma-associated obesity are orphan disorders that each afflict approximately 20K patients in the U.S. and EU. We estimate that beloranib could address a $1.5B+ opportunity in these two conditions. Behind beloranib, Zafgen is developing an orally active second-generation MetAP2 inhibitor, ZGN-839. ZGN-839 has shown early efficacy in preclinical models of Nonalcoholic Steatohepatitis (NASH) and type 2 diabetes. Zafgen plans to submit an IND for ZGN-839 in H1:15. 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. Today we are initiating coverage with an Outperform rating and a $45 price target.

Zafgen Upcoming Milestones

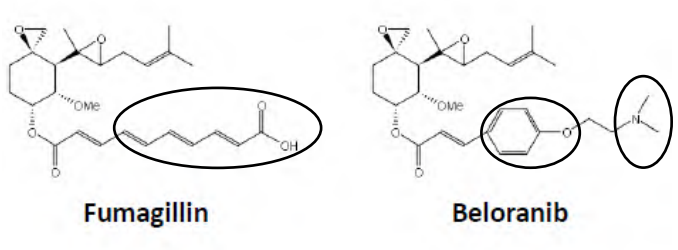
Milestone	Timing
Initiate Phase III trial of beloranib in PWS	H2:14
Initiate Phase IIb trial of beloranib in severe obesity	H2:14
Initial data from Phase IIa of beloranib in craniopharyngioma-associated obesity	Q1:15
File IND for ZGN-839 in type II diabetes, NASH and abdominal obesity	H1:15
Interim 6-month Phase IIb data from beloranib in severe obesity (complete Phase IIb; development decision point)	Q4:15
Phase III data from beloranib in PWS	Q4:15
Nomination of second-generation MetAP2i candidate	2016

Source: Cowen and Company

Beloranib (CKD-473): Make Me Better Than Fumagillin

Beloranib is a synthetic small molecule analog of fumagillin and is being developed by Zafgen as a novel, first-in-class injectable for the treatment of disease-associated obesities and hyperphagia. Fumagillin is a polyene macrolide antibiotic and a methionine aminopeptidase2 (MetAP2) inhibitor that was identified in 1949 from the microbial organism *Aspergillus fumigatus*. Efforts to develop fumagillin as an antibiotic concluded that it did not offer obvious benefits. However, subsequent research and the syntheses of novel analogs of fumagillin reignited medical community interest as these molecules exhibited anti-angiogenic effects. Fumagillin and its derivatives were studied to determine if they could inhibit blood vessel formations in cancers. Though fumagillin possessed interesting activities, it was not an ideal drug candidate. The long, double-bond-rich tail with a carboxylic acid group made fumagillin susceptible to oxidation and lowered its stability at room temperature. Chong Kun Dang (CKD) Pharmaceuticals substituted the unstable fumagillin tail with a benzene ring and an (N,N-dimethylaminoethyl) ethyl ether functional group and created CKD-473. Preclinical studies with CKD-473 showed improved pharmacokinetics and pharmacodynamics compared to fumagillin. CKD-473 was initially developed as an anti-angiogenic agent; however, its anti-obesity effects soon became apparent and clinical development focuses shifted almost immediately. In 2009, Zafgen signed an exclusive license agreement with CKD Pharmaceuticals and obtained worldwide rights to CKD-473 (beloranib) outside of South Korea.

Beloranib Is A Synthetic Analog Of Fumagillin



Source: Zafgen, Cowen and Company

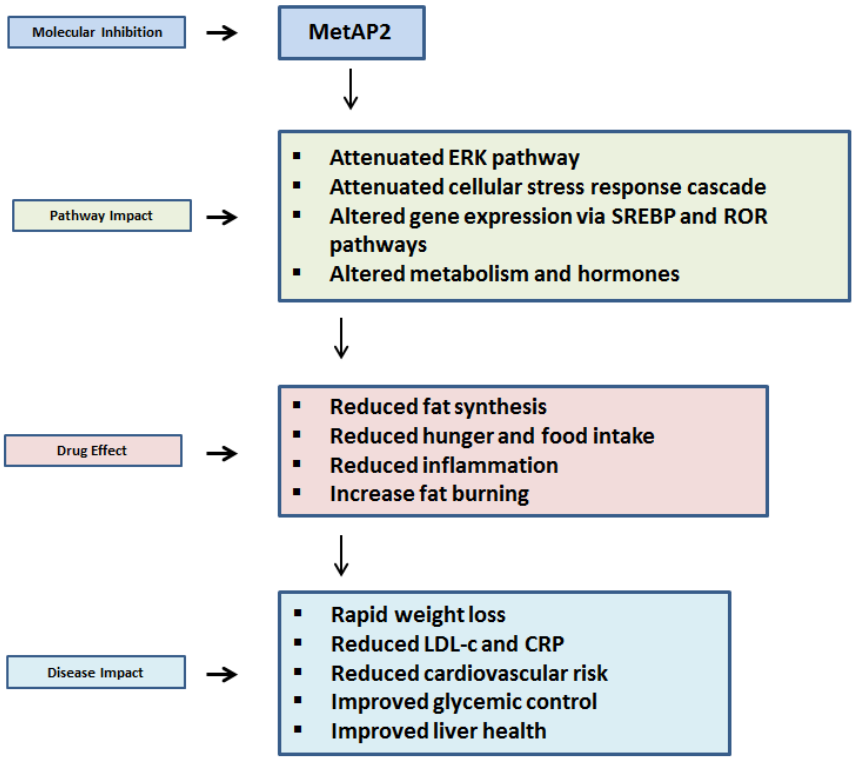
How Might Beloranib Work To Induce Weight Loss?

Beloranib attacks hyperphagia and weight loss by targeting the liver and adipose tissues in order to rebalance lipid metabolism and body composition, thereby reducing hunger. In lean people, the liver converts food into energy that is consumed by muscle. However, in the livers of obese people, food is persistently converted into stored fat that is not as readily metabolized. Beloranib redirects the metabolism of an obese patient so that it more resembles that of a lean person. Just as important for conditions characterized by hyperphagia (uncontrolled, insatiable appetite) such as Prader-Willi Syndrome (PWS) and craniopharyngioma, beloranib is able to dramatically reduce hunger and food intake.

As a synthetic derivative of fumagillin, beloranib achieves its anti-obesity effects, at least in part, through the inhibition of MetAP2. MetAP2 is an enzyme that removes the amino terminal methionine residue in newly synthesized proteins allowing for the synthesized protein to function properly. MetAP2 also affects cellular and metabolic processes by modulating protein network activities. While the precise pathways of the

anti-obesity effect of MetAP2 inhibitors are not well understood, genetic and molecular studies have implicated the non-enzymatic activities of MetAP2 as the likely mechanism. Inhibition of MetAP2 attenuates the cellular signaling that drives lipid synthesis by the liver and fat storage throughout the body.

MetAP2 Inhibitors Mechanism Of Action In Obesity

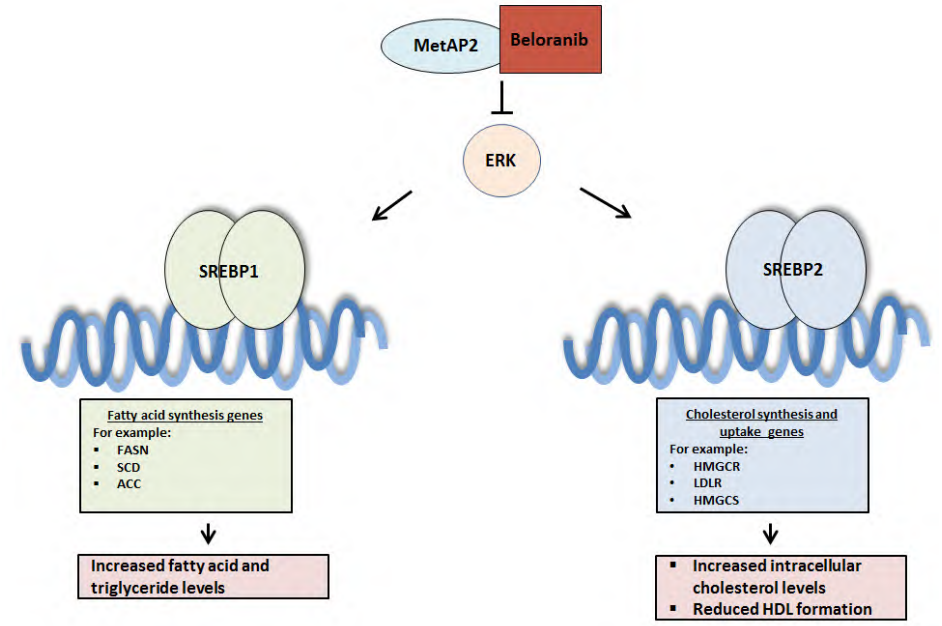


Source: Cowen and Company, Adapted from Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2014: 73-84

In 2004, fumagillin was found to induce binding between MetAP2 and an extracellular signal regulated kinase, ERK1. ERK1 is a well characterized enzyme that resides in the ERK pathway which mediates cellular stress and growth factor stimulation. Fumagillin was found to increase protein-protein interaction between MetAP2 and ERK1 which diminished ERK1 activity resulting in inhibition of cellular signaling cascades.

Research efforts have suggested that inhibition of ERK1 activity may provide benefits in metabolic abnormalities. Animal models that lacked ERK1 activity were resistant to high fat diet-induced obesity and avoided the development of insulin resistance. Furthermore, livers and adipose tissues from these animal models showed favorable gene expression changes when they were exposed to an extended fumagillin treatment. Consistent with current understandings of ERK-dependent cellular processes, reduction of ERK1 activity by MetAP2 inhibitors led to reductions in expression of gene factors involved in fatty acid and cholesterol synthesis and inflammation. One of the key targets of the ERK signaling pathway is the sterol regulatory element-binding protein (SREBP). SREBPs are transcription factors that regulate expression of proteins that mediate lipid biosynthesis and metabolism. Thus it seems likely that the beneficial effects of ERK inhibition with beloranib are amplified by the reduction of SREBP transcription activities.

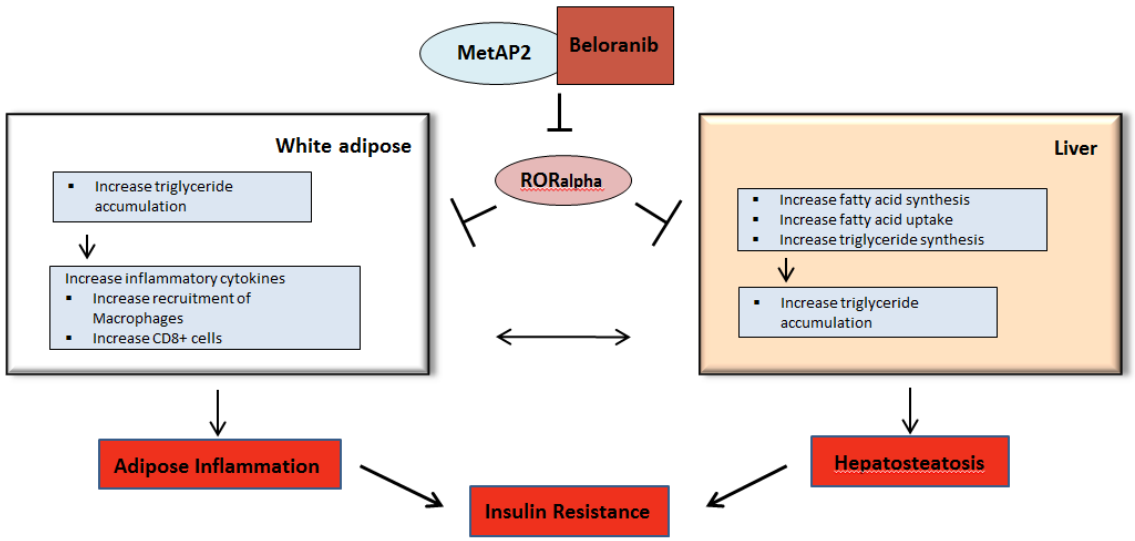
ERK And/Or SREBP Pathway



Source: Cowen and Company, Adapted from Rottiers V et. al. Nature Reviews Molecular Cell Biology 2012

Retinoic acid-receptor orphan receptors (RORs) mediated pathways are also targets of the ERK signaling pathway. RORs are a family of nuclear receptors that function as ligand-dependent transcription factors that mediate gene expressions including genes in the lipid and immune response pathways. RORs have also been found as key molecules that contribute to immune processes and diet- and age-induced obesity. Thus, suppression of ROR functions has been considered a way to protect against obesity and obesity-associated pathologies. Indeed, preclinical mouse models with deletion of proteins of the ROR family are protected against age- and diet-induced obesity and development of obesity-linked pathologies including adipose tissue-associated inflammation, hepatosteatosis and insulin resistance. Furthermore, transgenic obese mouse models with ROR gene deletions have also demonstrated rescue of obesity phenotypes with increased insulin sensitivity, and better glucose and lipid profiles.

RORs Mediate Obesity-Associated Pathologies



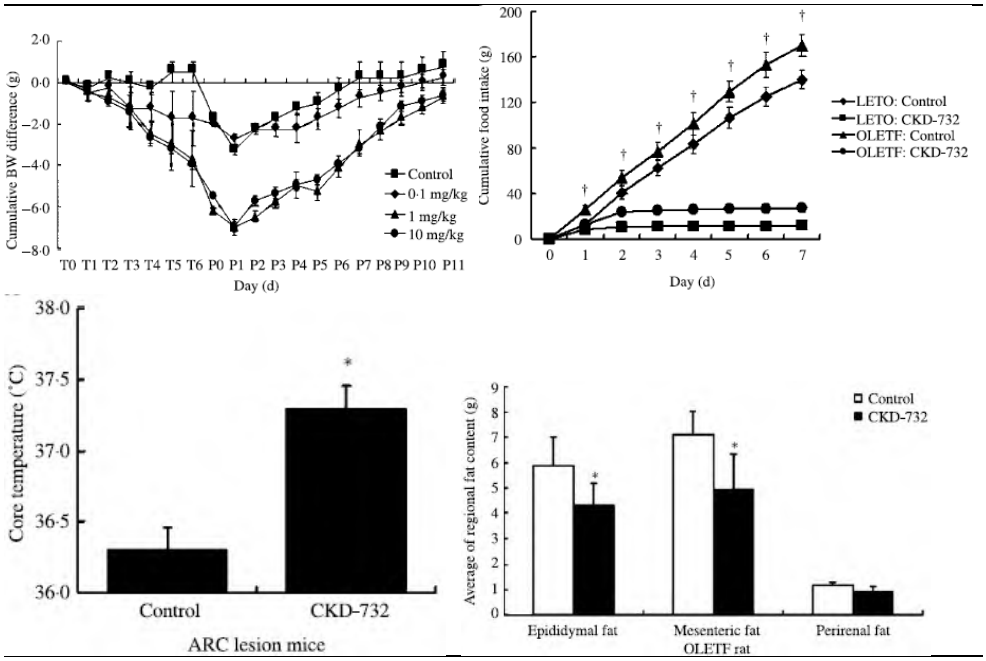
Source: Cowen and Company, Adapted from Jetten AM et. al. Frontiers In Endocrinology 2013

Beloranib is thought to antagonize the ERK pathway through a similar mechanism of action as fumagillin but with enhanced potency. Beloranib not only alters expression of genes in the metabolic pathway, it also induces hormones changes involved in energy metabolism. Zafgen believes that changes in hormones including leptin, adiponectin and fibroblast growth factor-21 observed in animal studies contribute to the rapid weight-reducing effects of beloranib. In addition to the weight loss efficacy, beloranib impacts the pathologies associated with obesity by showing improvements in glycemic control, reduced low density lipoprotein cholesterol, reduced inflammation mediator and biomarker C-reactive protein levels, and improvement of liver health.

Preclinical Studies With Beloranib

In preclinical in vitro studies, beloranib was found to possess higher affinity for MetAP2 and exhibited ~1000x more activity than the second most potent fumagillin derivative, TNP-470. Beloranib was investigated for its anti-obesity effects in rodent models of obesity. Seven days of beloranib subcutaneous injections resulted in rapid decrease in body weight loss in ARC mouse model of obesity and reduced cumulative food intake in OLETF/LETO rat models of obesity. Moreover, the weight loss effect was reversible, as body weights recovered after withdrawal of beloranib. Core temperature of ARC mice treated with beloranib was significantly higher than ARC mice treated with control, which suggests an increase in energy expenditure induced by beloranib. Further analyses found that weight loss in OLETF rats was due to significant reductions in epididymal and mesenteric fat pads.

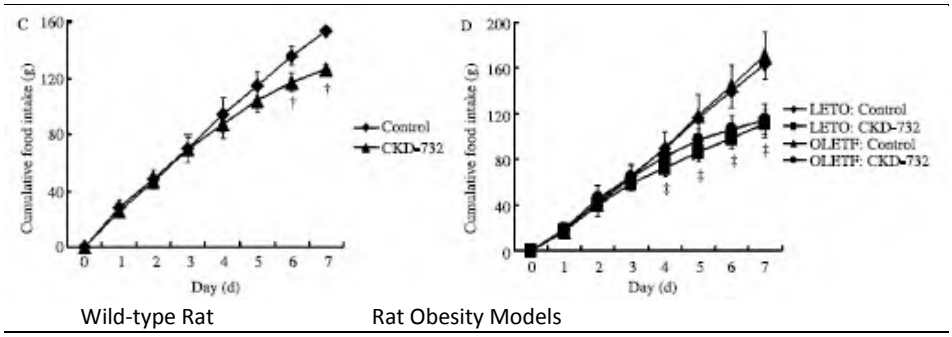
Beloranib Exert Rapid Effects In Rodent Models Of Obesity



Source: Zafgen

Interestingly, beloranib's effect on food-seeking behavior was specific to the rodent models of obesity as wild-type rodents exhibited minimal change in cumulative food intake.

Beloranib's Anti-Obesity Effects Are Amplified In Rat Obesity Models



Source: Zafgen

Zafgen has extended efficacy and toxicology studies from rodents to dogs and rabbits. Overall, beloranib was safe through dose levels ten to 15-fold above the doses utilized in Phase II clinical trials with male subjects. Moreover, the margins to the no adverse effect levels ranged from 40- to 60-fold higher in dogs and 50- to 100-fold higher in rats than the doses administered to female subjects in the clinical trials. At doses above human treatments, the most notable side effect was hypospermatogenesis, which was reversible with beloranib withdrawal.

Zafgen is completing long-term preclinical safety studies including 6-month studies in rats and nine-month studies in dogs. Long-term safety data will be used to support clinical trials of a year or more duration. Zafgen plans to complete these studies prior to the initiation of the Phase III study in PWS patients, and the Phase IIb trial in severe obesity. Zafgen has initiated dose-ranging studies in rodents in preparation for long-term carcinogenicity studies. Zafgen is also planning to conduct juvenile safety studies in 2014 to support beloranib's use in juvenile patients with PWS.

Phase I/II Trials Establish Proof Of Concept For Beloranib

Zafgen has completed five clinical trials in over 200 subjects including obese volunteers and Prader-Willi Syndrome patients. Through these trials Zafgen established 0.65 mg to 3 mg as the working dose range for beloranib with delivery via subcutaneous injections. Furthermore, beloranib has demonstrated early promises of efficacy as it has reduced fat mass and controlled hyperphagia while maintaining desirable tolerability and safety profiles.

Beloranib's Clinical Experience

Phase	Trial Name	Patient Population	Doses (plus Placebo)
Phase 1b (4 Wks Tx)	ZAF-001 ZAF-003	Post-menopausal or surgically sterile women BMI 30-50 kg/m^2	Up to 6 mg (*iv* route)
	ZAF-101	Post-menopausal, surgically sterile women or implanted contraception BMI 30-45 kg/m^2	0, 1, 2, 4 mg (*sc* route)
Phase 2a	ZAF-201 (12 Wks)	Men and post-menopausal, surgically sterile women or implanted contraception with or without type 2 diabetes. BMI 30-50 kg/m^2	0, 0.6, 1.2, 2.4 mg (*sc* route)
	ZAF-211 (4 Wks)	Men and women with Prader-Willi syndrome	0, 1.2, 1.8 mg (*sc* route)

Source: Zafgen

ZAF-001 - Phase Ib Study In Obese Subjects (IV)

Beloranib showed early promises in a four-week Phase Ib study initiated by Zafgen in December 2009. ZAF-001 was a randomized double-blinded, placebo-controlled dose escalation and multiple dose trial that evaluated primary endpoints including safety, tolerability, and PK and PD of beloranib. Obese but otherwise healthy female subjects with BMI range of 32-45 kg/m^2 were randomized into four different cohorts and received a total of six to eight intravenous infusions over a month period with beloranib at 0.1 mg/m^2, 0.3 mg/m^2, 0.9 mg/m^2 or placebo. In 26 evaluable subjects, treatment with beloranib at doses 0.9 mg/m^2, 0.3 mg/m^2 and 0.1 mg/m^2, led to a dose-dependent body weight reductions of 3.6 kg, 1.3 kg and 0.9 kg, respectively. In comparison, subjects in the placebo arm experienced a 1.2 kg weight loss. Though statistical analysis was not performed for the weight loss data, the apparent dose response is encouraging. Moreover, beloranib was well-tolerated with no reports of drug-related serious adverse events (SAEs) or treatment-emergent adverse events (TEAEs). The most common adverse events (AEs) reported were similar between the

beloranib treated group and the placebo group including headaches, GI symptoms and infusion site contusions or bruising.

ZAF-001 Phase Ib Weight Loss Efficacy Data

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)
Placebo	6	96.0	-1.2
Beloranib 0.1 mg/m^2	6	105.3	-0.9
Beloranib 0.3 mg/m^2	6	100.3	-1.3
Beloranib 0.9 mg/m^2	8	104.2	-3.6

Source: Zafgen

ZAF-003 Phase Ib Study Determined Maximum Dose Of Beloranib Tolerated By Obese Subjects (IV)

Beloranib continued to show promise in weight loss while demonstrating favorable safety in a Phase Ib study conducted by Zafgen in 2011. The maximum tolerated dose was also determined in this trial. ZAF-003 was a placebo-controlled, dose escalation, multiple dose, double-blinded and randomized study that enrolled 25 obese otherwise healthy subjects with BMI's ranging from 30 kg/m^2 to 50 kg/m^2. Subjects were randomized 2:1 into four cohorts to receive twice weekly intravenous infusions with 2.5 mg, 3.0 mg, 6.0 mg of beloranib or placebo. A total of 22 subjects completed the trial. Though statistical analysis was not performed, data trend showed subjects that received 3 mg or 6 mg of beloranib showed uniform weight loss and a reduction in hunger as assessed by a visual analog scale. Zafgen identified the maximally tolerated dose as 3.0 mg and eliminated the 6.0 mg dose in future trials since two subjects in the 6.0 mg cohort withdrew due to tolerability limitations. With the trial, Zafgen also determined that a once-weekly regimen with 2.5 mg of beloranib would be eliminated from future trials as it showed limited weight loss benefits or hunger reduction despite being well tolerated.

ZAF-003 Phase Ib Weight Loss Efficacy Data

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)
Placebo	8	104.6	-0.1
Beloranib 3.0 mg twice weekly	6	102.3	-4.7
Beloranib 6.0 mg twice weekly	3	105.5	-6.7
Beloranib 2.5 mg once weekly	5	94.0	-2.7

Source: Zafgen

ZAF-101 Phase IB Study With Beloranib Via Subcutaneous Injections (SC)

ZAF-101 was the first trial with beloranib formulated for delivery via subcutaneous injection. With this study, Zafgen showed for the first time treatment with beloranib led to a statistically significant weight loss. Zafgen also determined that the maximum tolerated dose of beloranib delivered subcutaneously is 4 mg. ZAF-101 enrolled and randomized 25 obese but otherwise healthy female subjects with BMI's of 30 kg/m^2 - 45 kg/m^2 into four groups at a ratio of 1:1:1:1. Patients received either placebo or

Beloranib at doses of 1.0 mg, 2.0 mg, and 4.0 mg delivered by subcutaneous injections twice weekly for four weeks. Subjects achieved an average weight loss reduction of 4.3 kg, 4.2 kg, and 6.1 kg ($p<0.001$) when treated with 1.0 mg, 2.0 mg and 4.0 mg of beloranib, respectively. In comparison, the placebo group experienced an average weight loss of 1.2 kg.

ZAF-101 Phase Ib Weight Loss Efficacy Data

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)	p-value
Placebo	6	97.3	-1.2	—
Beloranib 1.0 mg	6	99.1	-4.3	<0.001
Beloranib 2.0 mg	5	92.7	-4.2	<0.001
Beloranib 4.0 mg	4	93.9	-6.1	<0.001

Source: Zafgen

Zafgen reported that 4.0 mg appeared to be less well-tolerated and led to gastrointestinal events and sleep disturbances. Due to sleep disturbances, three patients from the 4.0 mg group and one patient from the 2.0 mg group withdrew prematurely from the trial. Sleep disturbances were the most common treatment-emergent adverse events with 85.7%, 100%, 83.3% and 16.7% of subjects reporting them at doses of 4.0 mg beloranib, 2.0 mg beloranib, 1.0 mg beloranib and placebo, respectively. The second most common AE reported was diarrhea, which occurred in 0%, 16.7% (1 event in 1 subject), 42.9% (3 events in 3 subjects) and 50% (3 events in 3 subjects) of the subjects treated with 1.0mg beloranib, 2.0mg beloranib, 4.0 mg beloranib and placebo, respectively. Nausea events reported were similar between the placebo and beloranib group.

Treatment Emergent Adverse Events In ZAF-101 Phase Ib Study

Trial Arm	# of Patients per Protocol	Sleep Disturbance Events (# of subjects)	# of Subjects with Sleep Abnormalities	# of Subjects with Mild Sleep Disorders	# of Diarrhea Events (# of subjects)	# of Nausea Events (# of subjects)
Placebo	6	1; 16.7% (1)	-	-	3 (3)	2 (2)
Beloranib 1.0mg	6	5; 83.3% (5)	4; 66.7%	6; 100%	-	1 (1)
Beloranib 2.0mg	5 + (1 withdrew)	6; 100% (5)	5; 83.3%	5; 83.3%	1 (1)	1 (1)
Beloranib 4.0mg	4 + (3 withdrew)	6; 85.7% (6)	6; 85.7%	33%	3 (3)	1 (1)

Source: Cowen and Company

ZAF-201 Phase IIa Study In Obese Subjects (SC)

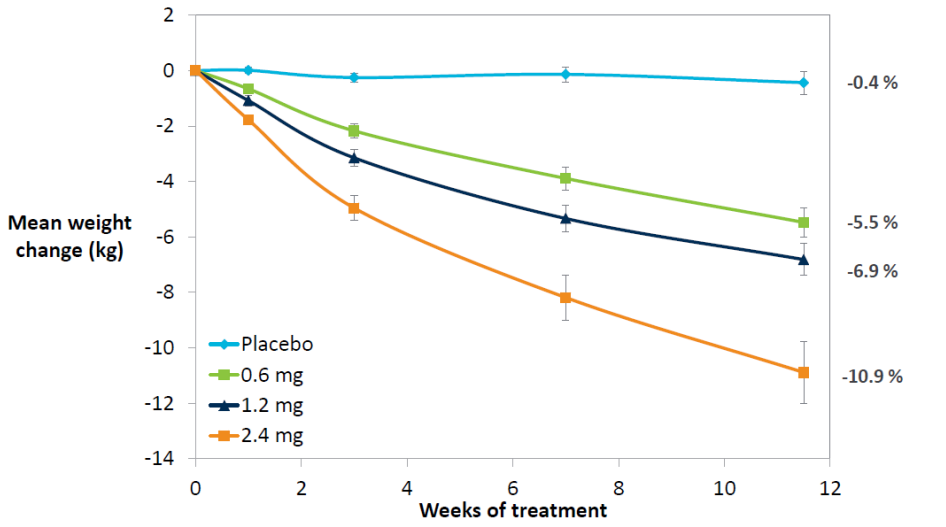
In May 2013, Zafgen completed a randomized double-blinded, placebo-controlled, dose-ranging Phase IIa trial that provided proof-of-concept for treatment of obese subjects with beloranib. The trial enrolled 160 obese but otherwise healthy subjects with BMI's of 30 kg/m^2 - 50 kg/m^2. Subjects had not recently been enrolled in a weight loss trial and all were considered eligible for bariatric surgery. Subjects were randomized into six different groups evaluating 0.3 mg, 0.6 mg, 1.2 mg, 2.4 mg, and 3.2 mg beloranib versus placebo. Beloranib and placebo were administered by subcutaneous injections twice weekly for 12 weeks. Endpoints assessed include

safety, tolerability, weight loss, responses in metabolic biomarkers and change from baseline in body weight and body composition.

A scheduled review occurred after 36 patients had been enrolled in the study. The Safety Review Committee recommended modifications to the protocol with elimination of the 0.3 mg and 3.2 mg treatment groups. The recommendation was based on the conclusion that the 3.2 mg dose had poor tolerability while the 0.3 mg dose did not produce sufficient weight loss. The trial was amended to test beloranib at doses of 0.6 mg, 1.2 mg, and 2.4 mg versus placebo.

Beloranib produced statistically significant weight loss. Subjects experienced a mean weight reduction of 5.5 kg, 6.9 kg and 10.9 kg with 0.6 mg, 1.2 mg, and 2.4 mg beloranib, respectively ($p<0.0001$). Meanwhile, subjects treated with placebo had a mean reduction of 0.4 kg. Zafgen noted that some patients in the 2.4 mg beloranib treatment group demonstrated 20% to 30% loss of body weight and achieved a BMI of 25 kg/m^2 at the end of the study. This level of weight loss is comparable to the benefits seen in surgical interventions with adjustable gastric banding or LapBand; however, without the increased risks and long-term complications due to the invasive nature of the surgical procedure.

ZAF-201 Phase IIa Trial - Dose-Dependent Mean Weight Reduction



Source: Zafgen

ZAF-201 Phase IIa Weight Loss Efficacy Data

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Mean Weight Change (kg)	Percent Placebo-Adjusted Weight Change	p-value
Placebo	36	102.3	-0.4	—	—
Beloranib 0.6 mg	34	102.6	-5.5	-5.0	<0.0001
Beloranib 1.2 mg	31	102.6	-6.9	-6.4	<0.0001
Beloranib 2.4 mg	15	102.2	-10.9	-10.3	<0.0001

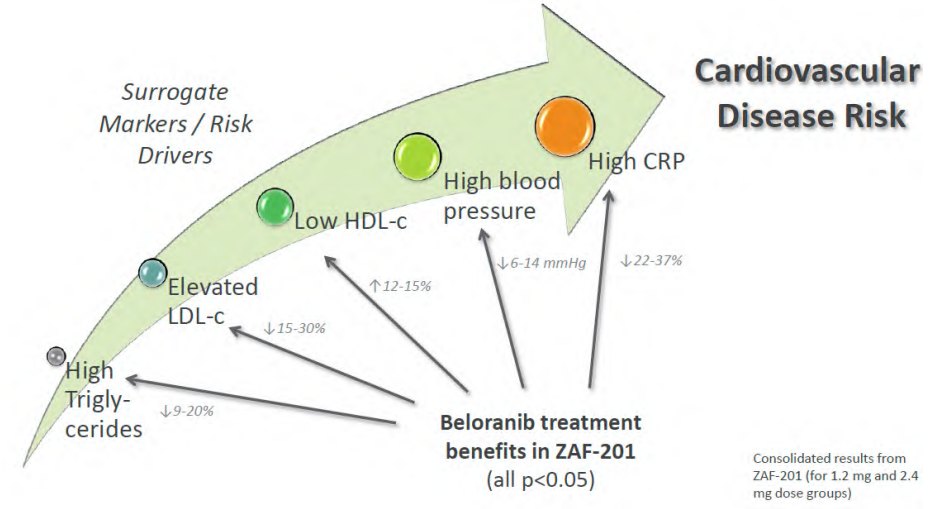
Source: Zafgen

Subjects' sense of hunger was assessed by a standardized visual analog scale with a maximum number of 10 cm. Beloranib led to a dose-dependent response with a reduction from baseline of 1.5 cm, 2.2 cm, and 3.3 cm with 0.6 mg, 1.2 mg, 2.4 mg, respectively versus the placebo arm with an average reduction from baseline of 0.1 cm.

Overall, treatment with 0.6 mg and 1.2 mg of beloranib was well tolerated and safe with most commonly reported treatment emergent adverse events (TEAEs) mild and transient. The most common TEAEs included sleep and gastrointestinal disorders. Zafgen noted that while the 2.4 mg cohort experienced the most rapid and significant weight loss, the cohort also experienced more tolerability issues compared to other doses, most specifically problems with sleep latency. Although problems falling asleep generally resolved during the first month of treatment, 21 subjects from the 2.4 mg cohort withdrew prematurely from the trial due to sleep disturbance issues. Sleep latency, or delayed time to falling asleep at night, was cited as the major cause for the subjects' decisions to withdraw from the trial. Two serious thrombotic events occurred, although neither was classified as related to beloranib treatment. Nonetheless, Zafgen may consider excluding patients with a prior history of thrombotic events from future studies, and may add vigilance for AEs related to blood clotting to the designs.

Treatment with beloranib at 1.2 mg and 2.4 mg led to significant benefits in cardiovascular biomarkers. Data from the 0.6 mg cohort also showed a favorable trend in subjects' cardiovascular status, although this trend did not achieve statistical significance. This suggests that beloranib treatment does not increase cardiovascular risks and may even reduce such risks. Treatment with beloranib reduced C-reactive protein (CRP) levels by approximately 22% to 37% ($p<0.0001$). Reductions in low density lipoprotein cholesterol (LDL-c) ranged from 9.4% to 29.7%. Beloranib increased high density lipoprotein cholesterol (HDL-c) by 7.6% to 14.6%. Reductions in triglycerides ranged from 8.8% to 20.3%. Systolic blood pressure also improved with statistically significant decreases ranging from 6.3% to 13.6% ($p<0.05$).

Beloranib Promotes Beneficial Cardiovascular Status



Source: Zafgen

ZAF-201 Systemic Biomarker Data

Trial Arm	CRP (µg/ml)	LDL-c (mmol/l)	HDL-c (mmol/l)	Triglycerides (mmol/l)	Systolic BP (mmHg)	Sense of Hunger (Baseline) (cm)
Placebo	+1.0***	-0.3	-	-0.3	-1.4	-0.1
Beloranib 0.6 mg	-2.5; -23%***	-0.3; -9.4%	+0.1; +7.6%	-0.2; -8.8%	-6.3	-1.5; (5.0)*
Beloranib 1.2 mg	-2.3; -22%***	-0.5; -14.5%	+0.1; +11.6%*	-0.3; -9.0%*	-6.3*	-2.2; (5.3)*
Beloranib 2.4 mg	-1.9; -37%***	-1.0; -29.7%**	+0.2; +14.6%*	-0.4; -20.3%*	-13.6*	-3.3; (6.4)*

CRP- C-reactive protein, LDL-c- low density lipoprotein cholesterol, HDL-c- high density lipoprotein cholesterol, BP- blood pressure; * p<0.05, ** p<0.001, *** p<0.0001

Source: Cowen and Company

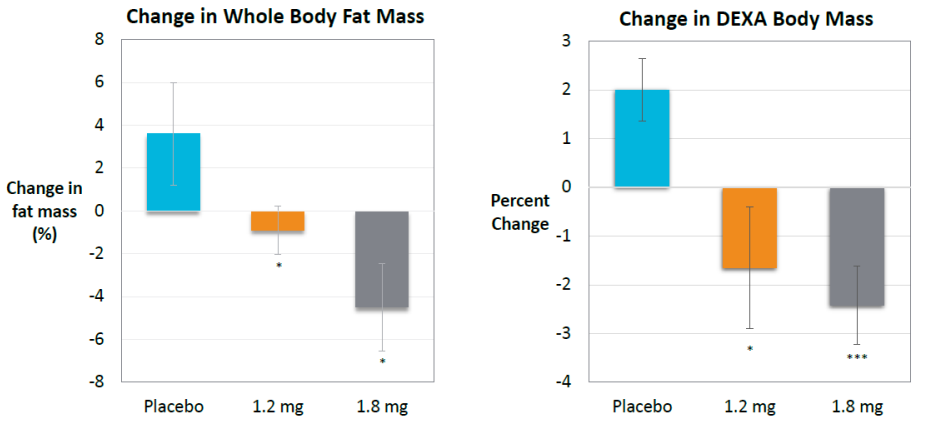
ZAF-211 Phase IIa Study In Patients With Prader-Willi Syndrome (SC)

In late 2013, Zafgen completed ZAF-211, a four-week Phase IIa proof of concept trial in patients with Prader-Willi Syndrome. The trial showed PWS patients treated with beloranib achieved statistically significant reductions in hyperphagia related behaviors, reductions in body and fat mass, and benefits in cardiovascular risk biomarkers.

ZAF-211 was a double-blinded, placebo-controlled, parallel dose ranging trial with 17 adult PWS patients living in closely controlled PWS-specific group homes. Patients were randomized to one of three dosing cohorts. The design of the trial incorporated a two-week placebo run-in. Patients were allowed to increase their daily caloric intake by 50% as Zafgen sought to simulate the environment of Prader-Willi patients living at home with their families where there is greater access to food. Placebo (n=6), 1.2 mg beloranib (n=5) and 1.8 mg beloranib (n=6) were administered twice weekly via subcutaneous injections. The primary endpoint of the trial was the percent change in body weight from baseline. Secondary endpoints include the changes in body weight from baseline and the changes in hyperphagia-related behaviors. After completion of the randomized trial phase, patients were given the option of continuing in a four-week open-label extension study.

Dual energy X-ray absorptiometry, DEXA, measurements showed beloranib treatment led to an average reduction of 2.1% in body mass versus a 2% gain in body mass in the placebo group ($p<0.002$). DEXA measurements also showed beloranib-treated patients lost on average 2.9% body fat while placebo group gained on average 3.6% body fat ($p<0.013$). Because of the increase in calories allowed in the trial, beloranib led to only a 1.3% decrease in weight, which was not statistically significant.

ZAF-211 Body Mass Reduction Efficacy Data



*, p<0.05; ***, p<0.005
Body composition and mass assessed by DEXA, dual-energy X-ray absorptiometry

Source: Zafgen

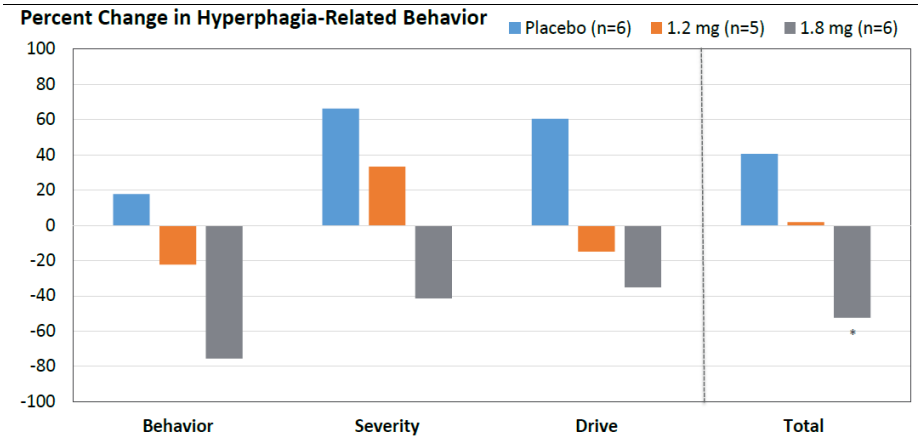
ZAF-211 Phase IIa Trial Weight Loss Efficacy Data

Endpoint	Placebo Baseline (N=6)	Placebo Change (%)	Beloranib Baseline (N=11)	Beloranib Change (%)	p value (Beloranib vs. Placebo)
Body weight (kg) (Scale weight)	70.1	0.34	72.0	-1.3	0.17*
Body mass (kg) (DEXA)	69.7	2.0	72.1	-2.1	0.002
Fat mass (kg) (DEXA)	31.1	3.6	34.6	-2.9	0.013

Source: Zafgen

Hyperphagia-related behaviors were assessed by the 13-item Prader-Willi Syndrome Hyperphagia Questionnaire. Hyperphagia-related behaviors reduced by an average of 52.4% in patients treated with 1.8 mg of beloranib, $p<0.05$. In comparison, patients treated with placebo had an average increase in hyperphagia-related behaviors of 40.5%. Patients treated with 1.2 mg of beloranib had an average increase of 1.8%.

ZAF-211 Dose Responsive Reduction In Hyperphagia-Related Behaviors



*, p<0.05

Reduction in behavior sub-scores were seen from baseline following randomized treatment with 1.8 mg beloranib

Source: Zafgen

PWS patients treated with beloranib also showed improved cholesterol profiles compared to the placebo treatment group. Beloranib treatment led to an average increase of 26% in HDL-c compared to an average increase of 1% in the placebo group (p=0.005). Concomitantly, the beloranib treatment group demonstrated a 27% decrease in LDL-c compared to an average increase of 3% in patients treated with placebo (p=0.005).

There were no SAEs reported in the trial and beloranib was demonstrated to be well-tolerated and safe in PWS patients, at the doses investigated in the study.

Phase III Study Ready for Initiation

Zafgen has held meetings with the FDA and the European Regulatory Authorities to discuss beloranib's pivotal program in Prader-Willi. Although discussions with the regulatory authorities continue, Zafgen currently expects the program will include two clinical trials, one in the U.S. and one in Europe, that will enroll a total of 240 patients 12 years of age or older with BMI's > 30 kg/m^2 and baseline hyperphagia scores of at least 13. Zafgen plans to initiate the U.S. Phase III trial during H2:14, with the European Phase III to start subsequently. The trials are expected to randomize patients to 1.8 mg beloranib, 2.4 mg beloranib or placebo. Patients will be dosed via subcutaneous injections twice weekly for six months, followed by a six months phase that may be either open label or randomized. The dual primary endpoint of the trial is improvement in total body fat mass and hyperphagia-related behaviors. In order for the trial to be considered a success either endpoint can be hit with statistical significance - the trial will be considered positive if either endpoint is hit with p<0.025, or if both are hit with p<0.05. The trial is 90% powered to demonstrate a 6% placebo-reduction in body fat mass, and a 20% placebo-adjusted reduction in hyperphagia. Secondary endpoints include body weight, LDL, HDL, and C-reactive protein. Zafgen expects to study PWS patients living in the family home setting in Phase III, as opposed to the PWS-specialized group home setting studied in Phase II. Zafgen is making progress in completing the work necessary to begin the Phase IIIs. The company is finishing pre-clinical animal studies, obtaining sufficient supply of

beloranib with the subcutaneous formulation, and validating instruments used for endpoint hunger measurements. Zafgen anticipates that initial six-month data will be available by Q4:15 from the Phase III study in the U.S.

In January 2013, beloranib received an Orphan Drug designation from the FDA for the treatment of PWS. Orphan designation for PWS was received from the European Commission in July 2014.

Prader-Willi Syndrome – A Rare And Severe Disease In Need Of New Treatments

Prader-Willi Syndrome is a devastating congenital orphan disease. While the exact genetic cause of PWS is not well understood, deletion or genetic imprinting (gene silencing methylation modifications) of several genes on the paternal Chromosome 15 (q11-13) is associated with the disease.

PWS has an estimated prevalence of between 1 in 8,000 to 1 in 50,000 in the U.S. and EU. PWS is characterized by cognitive, physiologic and behavioral symptoms that result in a very poor quality of life. PWS is not gender-specific, and afflicts approximately as many males as females. The clinical characteristics of PWS change as a child grows and develops. In infancy PWS patients often require ventilator support and feeding tubes to ensure survival due to severe hypotonia and feeding difficulties. During early childhood PWS patients' lives start to become dominated by hyperphagia. Hyperphagia describes a severe, insatiable appetite which often results in aggressive food-seeking, excessive eating and the development of morbid obesity. Developments of co-morbidities such as type II diabetes mellitus and sleep apnea often occur as a consequence of obesity. Cognitive disability and delayed motor milestone and language development are commonly associated with PWS during early childhood. Physically, PWS presents with hypoplasia, incomplete pubertal development and infertility due to hypogonadism. PWS patients also suffer from growth hormone insufficiencies which result in short stature. Characteristic dysmorphic facial features including strabismus and scoliosis are often present. In adulthood, PWS patients' lives are dominated by hyperphagia, resulting in a very poor quality of life. The hyperphagia behavior can require patients to live in a group home setting with limited access to food or to have around-the-clock supervision by a care-taker.

Prader-Willi Syndrome In Development

Phases	Median Ages	Clinical Characteristics
0	Prenatal To Birth	Decreased fetal movements and lower birth weight than siblings
1a	0 to 9 months	Hypotonia with difficulty feedings and decreased appetite
1b	9-25 months	Improved feeding and appetite and growing appropriately
2a	2.1 to 4.5 years	Weight increase without increase in appetite or excess calories
2b	4.5 to 8 years	Increased appetite and calories, but can feel full
3	8 years to adulthood	Hyperphagic, rarely feels full

Source: Cowen and Company, Adapted from Cassidy SB et. al. Genetics In Medicine 2012

Hyperphagia is defined as a powerful psychological and physiological drive to eat. Hypothalamic dysfunctions are thought to be the cause of the hyperphagia disorder in PWS. The hypothalamus functions as a central regulator of bodily functions including hunger, metabolism of carbohydrates and fats, sleep-wake cycle, body temperature

and expression of emotions. Hyperphagia often leads to extreme and risky food-seeking behaviors which require around-the-clock monitoring. Hyperphagia is also thought to be the underlying cause of obesity associated with PWS. Patients with PWS have abnormal satiety and will often consume 3x to 4x their daily recommended calories. The weight gain is compounded by the unwillingness of the patients to exercise as they lack energy and fatigue easily. Furthermore, patients are preoccupied with non-stop thoughts of food. Together, the increased food intake and the lack of energy expenditure exacerbate the weight gain and its associated co-morbidities. PWS patients often suffer from co-morbidities such as diabetes, poor cholesterol profiles, and cardiovascular diseases. The excessive food-seeking behavior is not only disruptive to the patient's day, it also leads to devastating effects on the patient's well-being, independence, health, and self-image. Left unattended, PWS patients will continuously seek and consume any obtainable food which can result in stomach rupture. Consequentially, caretakers are forced to put locks on food pantries and refrigerators and monitor the patient throughout the day. Many PWS patients are forced to live in specialized group homes.

Hyperphagia in PWS patients is evaluated by food diaries, measuring caloric intake, and the Prader-Willi Syndrome Hyperphagia Questionnaire. The Questionnaire is designed to provide factor-analytic and within-syndrome analysis measurements. The questionnaire comprises 13-items that assess food-seeking behaviors and risks of severe obesity.

A clinical diagnosis is almost always confirmed via blood test in suspected patients at around three months of age. "Methylation analysis" is the preferred laboratory test as it detects all major genetic subtypes of PWS including chromosome deletion, uniparental disomy, or imprinting mutations with an accuracy rate of 99%. Fluorescent in-situ hybridization (FISH) method is another test laboratory test available for PWS; however, it can only detect PWS due to deletions in chromosome 15.

Clinical Presentation Of Prader-Willi Syndrome

Major	Minor
-Neonatal / infantile hypotonia and poor suck	-Decreased fetal movement and infantile lethargy
-Feeding problems and failure to thrive as infant	-Typical behavior problems
-Weight gain at 1-6 years; obesity; hyperphagia	-Sleep apnea
-Characteristic dysmophic facial features	-Short stature for family by 15 years
-Small genitalia; pubertal delay and insufficiency	-Hypopigmentation for the family
-Developmental delay / intellectual disability	-Small hands and feet for height
	-Narrow hands, straight ulnar border
	-Esotropia, myopia
	-Thick, viscous saliva
	-Speech articulation defects
	-Skin picking

Source: Cowen and Company, Adapted from Cassidy SB et. al. Genetics In Medicine 2012

Current treatments available for PWS only manage disease symptoms as there are no effective pharmacological treatments for the underlying causes. Furthermore, there

are no treatments that can diminish or eliminate the hyperphagia that is characteristic of the disease. Though bariatric surgery has been shown to be very effective in the general obese population, in PWS patients it often leads to adverse effects. PWS patients who have had bariatric surgery have an increased risk of stomach rupture. Because of their hyperphagia these patients continue to eat large quantities of food, without feeling satiated. With a small stomach volume, reduced feelings of satiety and low sensitivity to pain, the patients can eat until their stomachs rupture, a potentially fatal complication. Thus, disease symptoms are mainly treated through diet and behavioral management and growth hormone therapy. Diet and behavioral management help to reduce calorie consumption and reduce food-seeking risks.

In 2000, the FDA approved human growth hormone for use in children with PWS. According to the Growth Hormone Research Society Workshop, the rationale behind growth hormone therapy is based on the understanding of the co-morbidities seen in PWS. While growth hormone does not treat the underlying disease, it does provide positive effects on development and behavior. Growth hormone treatment benefits the PWS patients by increasing height, stamina, bone mineral density, muscle mass with concomitant reduction in body fat resulting in improved weight distribution. However, growth hormone does not exert any impact on cognitive impairments, endocrine abnormalities, scoliosis, skin picking and most importantly, hyperphagia.

Consultants Think There Is Need For New Prader-Willi Treatments, And Are Impressed By Beloranib's Impact On Hyperphagia

Today, patients are treated through behavioral therapy, diet management, and growth hormone. Growth hormone is widely used in children with PWS as it increases height, muscle tone and other co-morbidities. Children who are maintained on growth hormone therapy and a stringent diet can avoid obesity. Although growth hormone does not increase height and has less impact on weight in adults, our consultants think it still improves adult patients' lives as they feel better and stronger. Reimbursement for growth hormone treatment in children is robust, but it remains costly and payors will often deny reimbursement for adults. While it has many benefits, growth hormone is far from a cure and in particular does not decrease hyperphagia. Many patients still need to be institutionalized despite behavioral and growth hormone therapy. Moreover, growth hormone can be associated with serious side effects such as the obstructive regrowth of adenoids, and, in rare cases, sudden death. Therefore our consultants still desire new agents.

Our consultants think controlling hyperphagia is the toughest challenge in treating PWS and craniopharyngioma-associated obesity. They note that no treatments are currently available for hyperphagia and that it is a significant unmet need. They attribute the low quality of life endured by patients and caretakers to hyperphagia. Our consultants think if hyperphagia is reduced, it would allow patients to live a more "normal" life and perhaps even allow them a measure of independence. Our consultants suggest that more patients may be able to leave group homes and to have the freedom to carry out "normal" day-to-day tasks. Moreover, it would also significantly reduce the burden of the caretakers. They believe weight loss and reductions in BMI are secondary benefits and can be achieved if hyperphagia is managed.

Our consultants think that beloranib's Phase II data in PWS is "impressive," and they are hopeful that it will be successfully developed. They find the impact of beloranib's 1.8mg dose on hyperphagia particularly meaningful. They think that should beloranib reduce hyperphagia by 50% in the real world, it would become standard of care,

appropriate for most patients. While our consultants note that the changes in body fat and body mass were not particularly large in Phase II, they think this is a result of the trial design. The Phase II was conducted in the group home setting where patients' weight and body fat was well controlled at baseline as they had all been on growth hormone and stringent diets for years.

Our consultants find beloranib's side effect profile acceptable. They say that sleep disturbances are well documented in Prader-Willi because of patients' reduced hypothalamic activity, and therefore the sleep disturbances noted in Phase II do not concern them. In fact, given that many Prader-Willi patients can experience daytime sleepiness, a bit of increase in sleep latency may be a benefit. Our consultants also note that beloranib's gastrointestinal side effects such as nausea, diarrhea, vomiting, and dizziness are commonly associated with many agents that impact weight (e.g. Byetta). Our consultants generally think that beloranib's administration via subcutaneous injection will not be a major impediment to use, as many patients are familiar with injections because of growth hormone treatment.

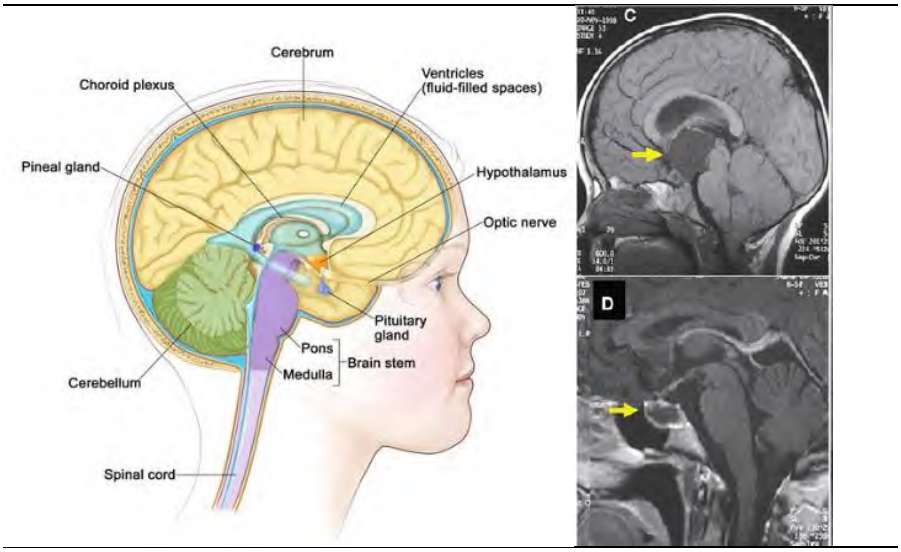
Based on the Phase II data, our consultants think it very likely that beloranib will succeed in its Phase III trial in Prader-Willi. They agree with Zafgen's decision to conduct the trial outside of the group home setting. They suggest that patients living in a family home are much more likely to be obese at baseline, and to have more prominent hyperphagia, as their access to food won't be nearly as restricted as that of institutionalized patients. To whit, in beloranib's Phase II the average BMI at baseline was 31 kg/m^2, and the average baseline score on the hyperphagia scale was 10 (out of 40 maximum). In Phase III Zafgen anticipates the average BMI will be 40-50 kg/m^2 at baseline, and the trial will exclude anyone with a baseline hyperphagia score of less than 13. Therefore, our consultants anticipate that the Phase III is likely to produce a more dramatic impact in body fat mass than the Phase II and expect to see at least as large of an impact on hyperphagia as in the Phase II. Our consultants think that the most prominent risk to beloranib's development in PWS is adverse events. While comfortable with beloranib's current adverse event profile, they note that a full evaluation of its safety must await completion of Phase III. They will pay particular attention to the risk of thrombosis in future trials. While generally convinced that the VTEs experienced in prior trials were not drug-related, they will be more certain once the Phase IIIs are completed.

Our consultants say that if beloranib can reduce hyperphagia by 50%, and should that effect be durable with long-term treatment, beloranib will be rapidly adopted in PWS. They would recommend therapy to all of their patients as they suggest beloranib would have real potential to improve patients' quality of life. A 10% change in total body fat mass would also be persuasive, and help drive uptake.

Craniopharyngioma – Associated Obesity

Craniopharyngioma-associated obesity is often referred to as "acquired PWS." Craniopharyngioma is a benign slow-growing tumor usually found near the pituitary gland and the hypothalamus. Craniopharyngioma frequently originates in the pituitary stalk and projects into the hypothalamus with the tumor expanding laterally along the path. Due to its growth pattern, craniopharyngioma is typically locally invasive with few metastatic cases documented. Surgical excision of the tumor, or pressure from the tumor itself, often disrupts brain functions mediated by the hypothalamus, pituitary gland, optic chiasm, optic nerves, and ventricles. Approximately 30% to 50% of diagnoses take place in children aged five to 14 years old via CT scan or MRI. Current estimated prevalence for the craniopharyngioma patient population is one in 50,000, with no known risk factors described.

Craniopharyngioma – Benign Tumor In The Brain



Source: National Cancer Institute, Zafgen

The onset of clinical presentations for craniopharyngioma is often described as insidious with headaches, endocrine deficiencies and visual disturbances as the most commonly reported symptoms. In children, endocrine deficiencies result in similar deficiencies as PWS with reduced production of growth hormone, gonadotropin, thyroid-stimulating hormone and corticotropin. As a result, patients are typically short in stature, obese and often experience precocious puberty.

Patients with craniopharyngioma are left with few options for treatment. The current treatment paradigm for craniopharyngioma involves surgical intervention to remove the tumor followed by radiation treatment. However, neighboring brain tissues such as the hypothalamus are often damaged as a result of the surgery and radiation treatment. It is estimated that approximately 50% of the craniopharyngioma patients treated by surgical intervention suffer from permanent damage to the hypothalamus. Patients with damage to the hypothalamus are at high risk for craniopharyngioma-associated obesity, including severe hyperphagia similar to that of a PWS patient.

Phase II Study In Craniopharyngioma Initiated

Zafgen initiated a Phase IIa trial in April 2014 to evaluate beloranib for the treatment of craniopharyngioma-associated obesity. The trial is expected to enroll a total of 14 obese patients due to radiographically confirmed hypothalamic damage with BMIs ranging from 30 to 60 kg/m^2. The primary endpoint will measure the change in body weight from baseline while secondary endpoints will assess changes in lipid profiles, changes from baseline in hunger and quality of life. Zafgen expects results to be available in Q1:15. Zafgen plans to subsequently conduct a Phase III in craniopharyngioma-associated obesity focused on weight loss, body composition changes and hunger reduction.

Physicians Hopeful That Beloranib Will Be Successfully Developed In Craniopharyngioma-Associated Obesity, Too

Our craniopharyngioma consultant suggests that the control of hyperphagia and weight remain key areas of unmet need in craniopharyngioma-associated obesity. She is impressed by beloranib's Phase II data in general obesity and PWS, and finds the reduction in hyperphagia from the PWS Phase II particularly striking. She thinks the data in PWS serve as reasonable proof of concept for beloranib's activity in craniopharyngioma, as both are hypothalamic conditions that result from structural abnormalities in the brain. Therefore she suggests it is likely that beloranib should produce a similar impact on hyperphagia and body composition in craniopharyngioma as in PWS.

Beloranib in Obesity

Obesity is a chronic condition affecting approximately one-third of the United States population, and its prevalence has doubled over the past two decades. Obesity is a complex disorder of metabolism and appetite regulation resulting in excessive adipose tissue mass accumulation. Typically, obesity is defined as a body mass index (BMI) of ≥30 kg/m^2. Obesity is a primary risk factor for the development of type 2 diabetes, hyperlipidemia, hypertension, and other cardiovascular disorders, and has been identified as the second most common factor contributing to preventable death behind tobacco use. Increased body weight also plays a role in the development of gallbladder disease, degenerative joint disease, respiratory disorders, and certain types of cancer. According to the Center for Disease Control (CDC), approximately 35.5% of the U.S. population is obese, which represents approximately 72 million people. In the EU, European Association For The Study Of Obesity estimates that approximately 20% of the population is obese, equating to approximately 32 million people. Together, the obese population in the U.S and EU account for more than 100 million people.

Body Mass Index (BMI)

	BMI (kg/m^2)	Obesity Class
Underweight	Below 18.5	
Healthy weight	18.5 to 24.9	
Overweight	25.0 to 29.9	
Mild Obesity	**30 to 34.9**	**I**
Moderate Obesity	**35 to 39.9**	**II**
Severe Obesity	**40 or higher**	**III**

Source: Cowen and Company, Centers for Disease Control

Because of the diverse mechanisms believed to underlie weight control, a broad array of approaches has been attempted to address this large and growing health care issue. Diet, increased physical activity, and behavioral modification are the mainstay strategies for weight loss and maintenance of healthy body weight. According to NIH guidelines on obesity treatment, pharmacotherapy may provide a beneficial adjunct to dietary activity and behavioral modifications in selected individuals, including: those with BMI ≥ 30 kg/m^2 (obese) and no concomitant risk factors, or those with BMI ≥ 27 kg/m^2 (overweight) and comorbidities such as hypertension, dyslipidemia, type 2 diabetes, coronary artery disease, and sleep apnea. For individuals with BMI 40 kg/m^2 (severely obese) bariatric surgery may be considered. However, serious medical complications associated with the surgical procedure and post-operative complications are common, including bleeding, thrombosis or embolism, infections,

and gastrointestinal obstructions, among others. Estimated rates for post-operative reoperations or conversion surgeries range from 17% to 31%. Per NIH recommendations, the initial goal of weight loss therapy is an approximately 10% reduction in body weight from baseline, accomplished within a time frame of 6 months on treatment.

Zafgen To Begin A Phase IIb Of Beloranib In Severe Obesity During H2:14

Zafgen plans to initiate a long-term Phase IIb study of beloranib in obesity during H2:14 based on the encouraging weight loss data generated in beloranib's Phase IIa. Zafgen expects to enroll both male and female patients with BMI's of up to 60 kg/m^2 and type 2 diabetes. The Phase IIb study is aimed at demonstrating six to 12 months of sustained weight loss with beloranib treatment. The trial will test two doses of beloranib, 1.2 mg and 1.8 mg. Zafgen expects to reduce AEs experienced during the first month of treatment such as sleep latency issues observed in the Phase IIa trial by utilizing a "fixed-titration" method. Patients on the higher dose will start at 1.2 mg, and be uptitrated to the 1.8 mg dose. Zafgen thinks that by tightly managing incremental dose escalations in individual subjects during the first month of dosing, the severity and frequency of AEs will be reduced significantly. Zafgen anticipates that preliminary six-month data will be available in Q4:15.

Preclinical Candidates Broaden Zafgen's Pipeline

Zafgen is developing other preclinical MetAP2 inhibitor candidates that have improved pharmacological and physicochemical features as potential follow-on compounds for beloranib. These include a second-generation MetAP2 inhibitor to be delivered via Sub-Q injection for obesity, and an orally active MetAP2 inhibitor for NASH and type 2 diabetes.

ZGN-839 - A Novel Class Of MetAP2 Inhibitor For NASH & Type 2 Diabetes Shows Early Promise In Preclinical Models

Zafgen has conducted a medicinal chemistry discovery program that has identified a reversible inhibitor of MetAP2, ZGN-839. ZGN-839 has improved bioavailability, and hence has the potential to be delivered orally. A synthetic manufacturing process for ZGN-839 is currently being developed, and ZGN-839 could enter clinical testing as early as H1:2015. Zafgen plans to investigate ZGN-839 in indications including nonalcoholic steatohepatitis (NASH), non-alcoholic fatty liver disease, abdominal obesity and type 2 diabetes.

In obese and insulin-resistant mouse models, treatment with ZGN-839 led to approximate 9% of body weight reduction, reduction of plasma cholesterol and glucose and concomitant improvements in liver fat and the weight of abdominal adipose tissues after only 16 days. Moreover, in mouse models of diabetes and NASH, treatment with ZGN-839 for four-weeks showed reduced severity of NASH and plasma glucose.

Zafgen expects to conduct IND-enabling studies for ZGN-839 during 2014 that will lead to an IND filing in the U.S in H1:2015.

Zafgen MetAP2 Inhibitor Pipeline Candidates

Drug Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Milestone
Beloranib Fumagillin-class MetAP2i	*Prader-Willi syndrome*	*Twice-weekly subcutaneous (SC) injection*				Initiate U.S. Phase 3 trial 2H 2014
Beloranib Fumagillin-class MetAP2i	*Cranio-pharyngioma*	*Twice-weekly subcutaneous injection*				Initiate Phase 2a trial 1H 2014
Beloranib Fumagillin-class MetAP2i	*Severe obesity*	*Twice-weekly subcutaneous injection*				Initiate Phase 2b trial 2H 2014
2nd Generation MetAP2i	*General obesity*	*SC Injection*				Candidate Nomination
ZGN-839 Novel chemical class MetAP2i	*NASH / Type 2 diabetes*	*Oral*				IND 1H 2015

Zafgen owns world-wide commercial rights to all compounds (exclusive of Korea for beloranib)

Source: Zafgen

Beloranib License And Intellectual Property

In July 2009, Zafgen signed an exclusive license agreement with Chong Kun Dang Pharmaceutical Corporation (CKD) and obtained worldwide rights to beloranib outside of South Korea. With the agreement, Zafgen paid an initial license fee and a one-time fee for the initiation of a proof-of-concept trial. Zafgen will also pay up to $30MM in milestone payments. If beloranib is successfully developed and commercialized, CKD is entitled to mid-to-high single-digit royalties on annual sales.

In January 2007, Zafgen and Children's Medical Center Corporation entered into an exclusive license agreement that provides Zafgen with exclusive worldwide patent rights for the use of beloranib and related molecules for decreasing the growth of fat tissues and as anti-obesity agents. Zafgen paid an initial license fee and annual maintenance fees through 2012. Children's is eligible to receive up to $2.7MM for the first licensed product, of which Zafgen has already paid $0.2MM. Children's is also eligible for up to $1.3MM for each subsequent product licensed, based on new chemical entity achievement milestones. Upon beloranib's approval by regulators, Children's is eligible to receive low single-digit royalties based on net sales through 2021.

Zafgen has built a solid patent portfolio around beloranib and additional patents are pending for the MetAP inhibitor programs. In the U.S., beloranib's composition of matter patent expires in 2019. Beloranib is protected by a polymorph composition of matter patent that expires in 2031. Zafgen has issued patents claiming methods of treating obesity with beloranib that expire in 2029. In the EU, Zafgen's composition of matter patent expires in 2019. Zafgen has more than 17 patents pending internationally, including eight patents pending for beloranib, seven patents pending related to the MetAP2 inhibitor program and two patents pending for the second-generation MetAP2 programs.

In addition to its patents, beloranib is also expected to be protected by orphan exclusivities in the U.S. and EU, which would last for 7 and 10 years, respectively, after approval. In January 2013 the FDA granted orphan designation for beloranib in Prader-Willi, and the European Commission granted orphan drug designation for beloranib in Prader-Willi in July 2014. Zafgen also plans to seek orphan drug designation for the treatment of craniopharyngioma-associated obesity in the U.S. and EU.

We Estimate That Beloranib Has $1B+ Revenue Potential

PWS – Prader-Willi Syndrome (PWS) is a rare disease with no patient registry currently available. Published population studies include a wide range of estimates for the prevalence of PWS, from 1 in 8,000 to 1 in 50,000 people in both the U.S. and EU. Physician consultants estimate the prevalence to be approximately 1 in 10,000 to 1 in 15,000, on the higher end of published estimates as our consultants note that the diagnosis is often missed. However, we have elected to use a conservative estimate of 1 in 40,000 in our model, implying that the number of PWS cases is 7,978 in the U.S. and 12,761 in the EU. We assume that half of the patients are 12 years or older, suggesting that 3,989 patients in the U.S. and 6,380 patients in the EU are available for treatment with beloranib.

We project beloranib will be launched in 2017 in the U.S. and 2018 in the EU. We model a ramp starting with 5% market penetration in 2017 and peak penetration of 37% in 2031 in the U.S. Meanwhile, in the EU we model a ramp starting at 5% penetration in 2018 with peak penetration of 32% in 2031. Management has suggested a monthly treatment price of ~$10,000/patient in the U.S and ~$7,500/patient in the EU. Therefore, we model U.S. PWS sales of $25MM in 2017 increasing to $400MM in 2031 and EU PWS sales of $20MM in 2018 increasing to $375MM in 2031.

Craniopharyngioma –Craniopharyngioma-associated obesity, similar to PWS, is rare and has an estimated prevalence of approximately 1 in 8,000 to 1 in 50,000. We assume a prevalence of 1:40,000 patients in the U.S. and EU, again on the lower end of estimates. Our physician consultant estimates that about 50% of the craniopharyngioma patients are suitable for treatment with beloranib. We estimate that there are 7,978 patients with craniopharyngioma-associated obesity in the U.S., of whom 3,989 are suitable for beloranib. In the EU, we estimate that there are 12,761 cases of craniopharyngioma-associated obesity, of whom 6,380 are eligible for treatment with beloranib.

We project that beloranib will launch in 2018 in the U.S. and 2019 in the EU for craniopharyngioma. We model peak market penetration of 35% in the U.S. and 28% in the EU in 2031. Our model assumes an initial market penetration of 5% in 2018 for the U.S and 2019 in the EU. With a suggested monthly treatment price of ~$10,000/patient in the U.S and ~$7,500/patient in the EU, we model U.S. craniopharyngioma sales of $25MM in 2018 increasing to $375MM in 2031 and EU craniopharyngioma sales of $20MM in 2019 increasing to $335MM in 2031.

In total, our model projects worldwide sales of beloranib in craniopharyngioma and PWS of $25MM in 2017, growing to $1.49B in 2031. Our model contains no assumptions for the use of beloranib in obesity in the general population, a potential source of upside. We also do not model any revenue from sales of Zafgen's preclinical candidates.

Beloranib Revenue Model

US beloranib Revenue Model	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Prader-Willi																		
US population	319,106,915	321,564,038	324,040,081	326,535,190	329,049,511	331,583,192	334,136,383	336,709,233	339,301,894	341,914,519	344,547,260	347,200,274	349,873,716	352,567,744	355,282,516	358,018,191	360,774,931	363,552,898
Population growth	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*
Prevalence of Prader-Willi Syndrome (PWS)	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*
# of cases of PWS	7,978	8,039	8,101	8,163	8,226	8,290	8,353	8,418	8,483	8,548	8,614	8,680	8,747	8,814	8,882	8,950	9,019	9,089
% of pateints that are 12 years or older	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of cases of PWS that are 12 years or older	3,989	4,020	4,051	4,082	4,113	4,145	4,177	4,209	4,241	4,274	4,307	4,340	4,373	4,407	4,441	4,475	4,510	4,544
% beloranib penetration				*5%*	*10%*	*15%*	*20%*	*24%*	*28%*	*31%*	*32%*	*32%*	*34%*	*35%*	*36%*	*36%*	*37%*	*37%*
# of patients treated with beloranib				208	397	605	828	1,028	1,208	1,306	1,362	1,410	1,477	1,535	1,584	1,624	1,657	1,684
Cost of treatment/month				$10,000	$10,500	$11,025	$11,576	$12,155	$12,763	$13,401	$14,071	$14,775	$15,513	$16,289	$17,103	$17,959	$18,856	$19,799
% price increase				*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
Duration of treatment (months)				12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Total US Sales in Prader-Willi ($MM)	$0	$0	$0	$25	$50	$80	$115	$150	$185	$210	$230	$250	$275	$300	$325	$350	$375	$400
% increase y/y					*100%*	*60%*	*44%*	*30%*	*23%*	*14%*	*10%*	*9%*	*10%*	*9%*	*8%*	*8%*	*7%*	*7%*
Craniopharyngioma-Associated Obesity																		
Prevalence of craniopharyngioma-associated obesity	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*
# cases of craniopharyngioma-associated obesity	7,978	8,039	8,101	8,163	8,226	8,290	8,353	8,418	8,483	8,548	8,614	8,680	8,747	8,814	8,882	8,950	9,019	9,089
% of craniopharyngioma patients eligible for treatment with	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of craniopharyngioma patients eligible for treatment with beloranib	3,989	4,020	4,051	4,082	4,113	4,145	4,177	4,209	4,241	4,274	4,307	4,340	4,373	4,407	4,441	4,475	4,510	4,544
% beloranib penetration					*5%*	*9%*	*14%*	*19%*	*23%*	*27%*	*29%*	*30%*	*31%*	*32%*	*33%*	*34%*	*34%*	*35%*
# of patients treated with beloranib				-	198	378	576	788	979	1,150	1,244	1,297	1,343	1,407	1,462	1,508	1,547	1,578
Cost of treatment/month				$10,000	$10,500	$11,025	$11,576	$12,155	$12,763	$13,401	$14,071	$14,775	$15,513	$16,289	$17,103	$17,959	$18,856	$19,799
% price increase				*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
Duration of treatment (months)				12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Total US Sales in craniopharyngioma-associated obesity ($MM)	$0	$0	$0	$0	$25	$50	$80	$115	$150	$185	$210	$230	$250	$275	$300	$325	$350	$375
% increase y/y						*100%*	*60%*	*44%*	*30%*	*23%*	*14%*	*10%*	*9%*	*10%*	*9%*	*8%*	*8%*	*7%*
Total US sales ($MM)	**$0**	**$0**	**$0**	**$25**	**$75**	**$130**	**$195**	**$265**	**$335**	**$395**	**$440**	**$480**	**$525**	**$575**	**$625**	**$675**	**$725**	**$775**

EU beloranib Revenue Model	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Prader-Willi																		
EU population	510,435,295	511,507,209	512,581,374	513,657,795	514,736,476	515,817,423	516,900,640	517,986,131	519,073,902	520,163,957	521,256,301	522,350,939	523,447,876	524,547,117	525,648,666	526,752,528	527,858,708	528,967,212
Population growth	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*	*0.21%*
Prevalence of Prader-Willi Syndrome (PWS)	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*
# of cases of PWS	12,761	12,788	12,815	12,841	12,868	12,895	12,923	12,950	12,977	13,004	13,031	13,059	13,086	13,114	13,141	13,169	13,196	13,224
% of pateints that are 12 years or older	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of cases of PWS that are 12 years or older	6,380	6,394	6,407	6,421	6,434	6,448	6,461	6,475	6,488	6,502	6,516	6,529	6,543	6,557	6,571	6,584	6,598	6,612
% beloranib penetration					*3%*	*8%*	*12%*	*16%*	*20%*	*24%*	*25%*	*26%*	*27%*	*29%*	*30%*	*31%*	*31%*	*32%*
# of patients treated with beloranib	-	-	-	-	212	504	768	1,051	1,306	1,534	1,658	1,730	1,791	1,876	1,949	2,011	2,062	2,104
Cost of treatment/month				$7,500	$7,875	$8,269	$8,682	$9,116	$9,572	$10,051	$10,553	$11,081	$11,635	$12,217	$12,828	$13,469	$14,142	$14,849
% price increase				*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
Duration of treatment (months)				12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Total EU Sales ($MM)	$0	$0	$0	$0	$20	$50	$80	$115	$150	$185	$210	$230	$250	$275	$300	$325	$350	$375
% increase y/y						*150%*	*60%*	*44%*	*30%*	*23%*	*14%*	*10%*	*9%*	*10%*	*9%*	*8%*	*8%*	*7%*
Craniopharyngioma-Associated Obesity																		
Prevalence of craniopharyngioma-associated obesity	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*	*0.00%*
# cases of craniopharyngioma-associated obesity	12,761	12,788	12,815	12,841	12,868	12,895	12,923	12,950	12,977	13,004	13,031	13,059	13,086	13,114	13,141	13,169	13,196	13,224
% of craniopharyngioma patients eligible for treatment with	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of craniopharyngioma patients eligible for treatment with beloranib	6,380	6,394	6,407	6,421	6,434	6,448	6,461	6,475	6,488	6,502	6,516	6,529	6,543	6,557	6,571	6,584	6,598	6,612
% beloranib penetration						*3%*	*7%*	*11%*	*15%*	*20%*	*22%*	*25%*	*26%*	*27%*	*27%*	*28%*	*28%*	*28%*
# of patients treated with beloranib				-	-	202	480	731	1,001	1,285	1,461	1,617	1,683	1,739	1,787	1,825	1,856	1,880
Cost of treatment/month				$7,500	$7,875	$8,269	$8,682	$9,116	$9,572	$10,051	$10,553	$11,081	$11,635	$12,217	$12,828	$13,469	$14,142	$14,849
% price increase				*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
Duration of treatment (months)				12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Total EU Sales in craniopharyngioma-associated obesity ($MM)	$0	$0	$0	$0	$0	$20	$50	$80	$115	$155	$185	$215	$235	$255	$275	$295	$315	$335
% increase y/y							*150%*	*60%*	*44%*	*35%*	*19%*	*16%*	*9%*	*9%*	*8%*	*7%*	*7%*	*6%*
Total EU sales ($MM)	**$0**	**$0**	**$0**	**$0**	**$20**	**$70**	**$130**	**$195**	**$265**	**$340**	**$395**	**$445**	**$485**	**$530**	**$575**	**$620**	**$665**	**$710**
Total US/EU sales ($MM)	**$0**	**$0**	**$0**	**$25**	**$95**	**$200**	**$325**	**$460**	**$600**	**$735**	**$835**	**$925**	**$1,010**	**$1,105**	**$1,200**	**$1,295**	**$1,390**	**$1,485**

Source: Cowen and Company.

DCF Analysis Suggests That Zafgen Is Undervalued On The Potential of Beloranib In PWS And Craniopharyngioma

We have incorporated our beloranib revenue and Zafgen expense estimates into a DCF. Briefly, we assume beloranib is launched in 2017 in the U.S. and 2018 in the EU and achieves $1B in revenue by 2026. We assume it grows to $1.49B in 2031, and declines following the expiration of its patents. We assume that Zafgen's R&D expense grows from $36MM in 2014 to $70MM in 2020, and that its SG&A increases from $5MM in 2014 to $75MM by 2020. Our model assumes that Zafgen breaks into profitability in 2019 following the launch of beloranib in both U.S. and EU. Our DCF does not include any revenue from other indications such as severe obesity. We apply a 12% discount rate, and a 0% terminal growth rate. Our analysis suggests that beloranib in PWS and craniopharyngioma is worth $45/share, with no contribution from beloranib in obesity or the rest of Zafgen's pipeline.

Zafgen DCF Analysis

Financial Year End	12/31/2014
Valuation Date	7/9/2014
Discount Rate	**12.0%**
Terminal Growth Rate	**0.0%**

ZAFGEN: DCF Valuation

$MM	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Beloranib				25	95	200	325	460	600	735	835	925	1010	1105	1200	1295	1390	1485
Growth (%)					*280%*	*111%*	*63%*	*42%*	*30%*	*23%*	*14%*	*11%*	*9%*	*9%*	*9%*	*8%*	*7%*	*7%*
License/milestones revenue	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Growth (%)																		
Total Revenues	**0**	**0**	**0**	**25**	**95**	**200**	**325**	**460**	**600**	**735**	**835**	**925**	**1010**	**1105**	**1200**	**1295**	**1390**	**1485**
Growth (%)									*30%*	*23%*	*14%*	*11%*	*9%*	*9%*	*9%*	*8%*	*7%*	*7%*
COGS	**0**	**0**	**0**	**2**	**7**	**13**	**20**	**46**	**60**	**66**	**75**	**83**	**91**	**99**	**108**	**117**	**125**	**134**
COGS as a % of sales				**8%**	7%	7%	6%	*10%*	*10%*	9%	9%	9%	9%	9%	9%	9%	9%	9%
R&D	**36**	**43**	**50**	**75**	**60**	**65**	**70**	**92**	**120**	**110**	**104**	**93**	**51**	**55**	**60**	**65**	**70**	**74**
R&D as a % of Revenues				*300%*	*63%*	*33%*	*22%*	*20%*	*20%*	*15%*	*13%*	*10%*	*5%*	*5%*	*5%*	*5%*	*5%*	*5%*
SG&A	**5**	**13**	**29**	**40**	**50**	**60**	**75**	**92**	**120**	**147**	**167**	**185**	**202**	**221**	**240**	**259**	**278**	**297**
SG&A as a % of Revenues				*160%*	*53%*	*30%*	*23%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*	*20%*
Operating Income	**-42**	**-56**	**-79**	**-92**	**-22**	**62**	**161**	**230**	**300**	**412**	**488**	**564**	**667**	**729**	**792**	**855**	**917**	**980**
Tax	**0**	**0**	**0**	**0**	**0**	**0**	**56**	**81**	**105**	**144**	**171**	**197**	**233**	**255**	**277**	**299**	**321**	**343**
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
NOL/Tax Assets Utilized																		
Tax rate																		
Taxes Paid	**0**	**0**	**0**	**0**	**0**	**0**	**56**	**81**	**105**	**144**	**171**	**197**	**233**	**255**	**277**	**299**	**321**	**343**
Approx Free Cash Flow	**(42)**	**(56)**	**(79)**	**(92)**	**(22)**	**62**	**104**	**150**	**195**	**268**	**318**	**367**	**433**	**474**	**515**	**556**	**596**	**637**
Years	0.48	1.47	2.48	3.48	4.48	5.47	6.48	7.48	8.48	9.47	10.48	11.48	12.47	13.47	14.48	15.48	16.47	17.47
Discount Factor	0.95	0.85	0.76	0.67	0.60	0.54	0.48	0.43	0.38	0.34	0.31	0.27	0.24	0.22	0.19	0.17	0.15	0.14
NPV of Cash flows	**(39)**	**(47)**	**(60)**	**(62)**	**(13)**	**33**	**50**	**64**	**75**	**91**	**97**	**100**	**105**	**103**	**100**	**96**	**92**	**88**

Terminal Value Calculation

Final year FCF	637
Perpetual Growth Rate	0.0%
Terminal Value	**0**
Discount Factor	0.14
Present Value of Terminal Value	**0**
Present Value of Cash Flows	**913**
Enterprise Value	**913**
Add: Net cash	110
Market Value	**1,023**
Fully Diluted Shares Outstanding	22.7
Value per Fully Diluted Share	**$45.08**

Source: Cowen and Company

Zafgen Quarterly P&L ($MM)

	Q1:14A	Q2:14E	Q3:14E	Q4:14E	2014E	Q1:15E	Q2:15E	Q3:15E	Q4:15E	2015E
Boleranib	-	-	-	-	-	-	-	-	-	-
License/milestones revenue	-	-	-	-	-	-	-	-	-	-
Total Revenue	-	-	-	-	-	-	-	-	-	-
COGS	-	-	-	-	-	-	-	-	-	-
R&D	3.3	5.5	17.8	9.5	36.1	10.0	10.5	11.0	11.5	43.0
SG&A	1.2	1.3	1.4	1.5	5.4	1.8	2.5	3.5	5.0	12.8
Other	-	-	-	-	-					-
Operating Expenses	4.5	6.8	19.2	11.0	41.5	11.8	13.0	14.5	16.5	55.8
Operating Income / (Loss)	(4.5)	(6.8)	(19.2)	(11.0)	(41.5)	(11.8)	(13.0)	(14.5)	(16.5)	(55.8)
Interest Income	-	0.1	0.1	0.1	0.3	0.1	0.1	0.1	0.1	0.4
Interest Expenses	(0.0)	(0.0)	(0.0)	(0.0)	(0.1)	(0.4)	(0.4)	(0.4)	(0.4)	(1.6)
Foreign Currency Transaction Gains (Losses), n	0.1	-	-	-	0.1	-	-	-	-	-
Pretax net income	(4.5)	(6.7)	(19.1)	(10.9)	(41.3)	(12.1)	(13.3)	(14.8)	(16.8)	(57.0)
Accretion of redeemable convertible preferred st	(0.0)	-	-	-	-	-	-	-	-	-
Taxes	-	-	-	-	-	-	-	-	-	-
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
GAAP Net Income	(4.5)	(6.7)	(19.1)	(10.9)	(41.3)	(12.1)	(13.3)	(14.8)	(16.8)	(57.0)
GAAP EPS	**$ (0.98)**	**$ (0.43)**	**$ (0.84)**	**$ (0.48)**	**$ (2.50)**	**$ (0.52)**	**$ (0.57)**	**$ (0.64)**	**$ (0.72)**	**$ (2.45)**
Diluted Shares Outstanding (MM)	4.6	15.8	22.7	22.9	16.5	23.0	23.2	23.3	23.4	23.2

Source: Cowen and Company

Zafgen Annual P&L ($MM)

	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Boleranib	-	-	-	-	25.0	95.0	200.0	325.0
License/milestones revenue	-	-	-	-	-	-	-	-
Total Revenue	-	-	-	-	25.0	95.0	200.0	325.0
COGS	-	-	-	-	2.0	6.8	13.0	19.5
R&D	9.6	36.1	43.0	50.0	75.0	60.0	65.0	70.0
SG&A	4.2	5.4	12.8	29.0	40.0	50.0	60.0	75.0
Other	-	-	-	-	-	-	-	-
Operating Expenses	13.8	41.5	55.8	79.0	117.0	116.8	138.0	164.5
Operating Income / (Loss)	(13.8)	(41.5)	(55.8)	(79.0)	(92.0)	(21.8)	62.0	160.5
Interest Income	-	0.3	0.4	0.3	0.8	0.8	0.4	0.9
Interest Expenses	-	(0.1)	(1.6)	(0.8)	(0.4)	-	-	-
Foreign Currency Transaction Gains (Losses), net	(0.2)	0.1	-	-	-	-	-	-
Pretax net income	(14.0)	(41.3)	(57.0)	(79.5)	(91.6)	(21.0)	62.4	161.4
Accretion of redeemable convertible preferred stoc	(0.2)	-	-	-	-	-	-	-
Taxes	-	-	-	-	-	-	-	-
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
GAAP Net Income	(14.2)	(41.3)	(57.0)	(79.5)	(91.6)	(21.0)	62.4	161.4
GAAP EPS	**$ (3.11)**	**$ (2.50)**	**$ (2.45)**	**$ (2.75)**	**$ (3.10)**	**$ (0.70)**	**$ 2.05**	**$ 5.20**
Diluted Shares Outstanding (MM)	4.6	16.5	23.2	28.9	29.5	29.8	30.4	31.0

Source: Cowen and Company

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
BMRN	BioMarin Pharmaceutical
GILD	Gilead Sciences
PTLA	Portola Pharmaceuticals
ZFGN	Zafgen

Analyst Certification

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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 Dahlman Rose & Company, Rating System until May 25, 2013

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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

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Distribution of Ratings/Investment Banking Services (IB) as of 06/30/14

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	417	58.57%	94	22.54%
Hold (b)	279	39.19%	7	2.51%
Sell (c)	16	2.25%	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.

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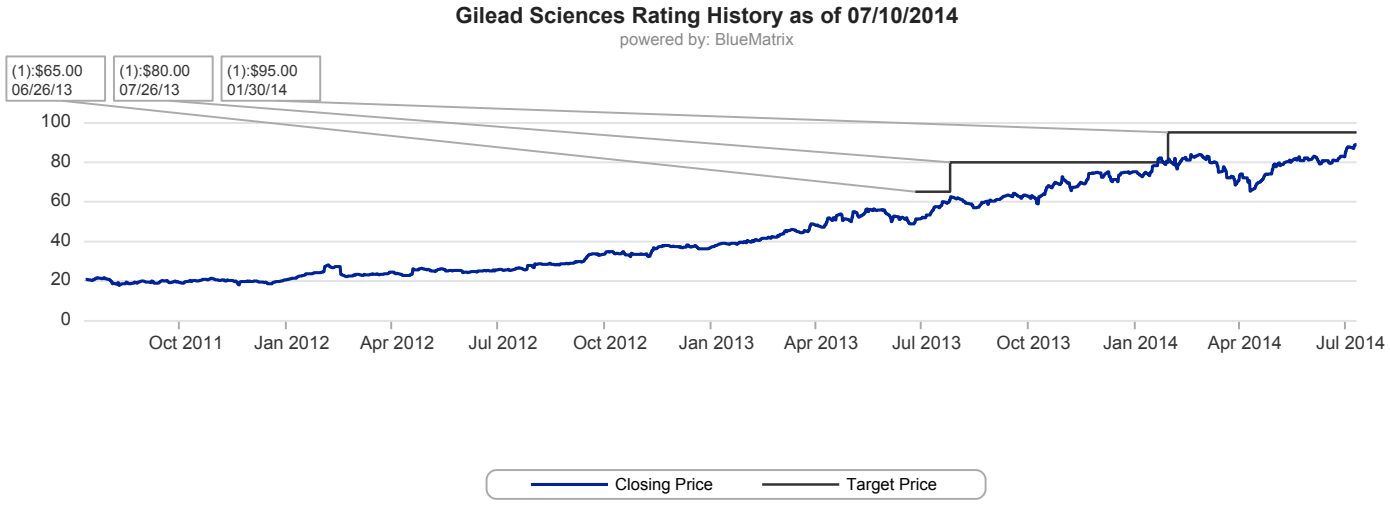

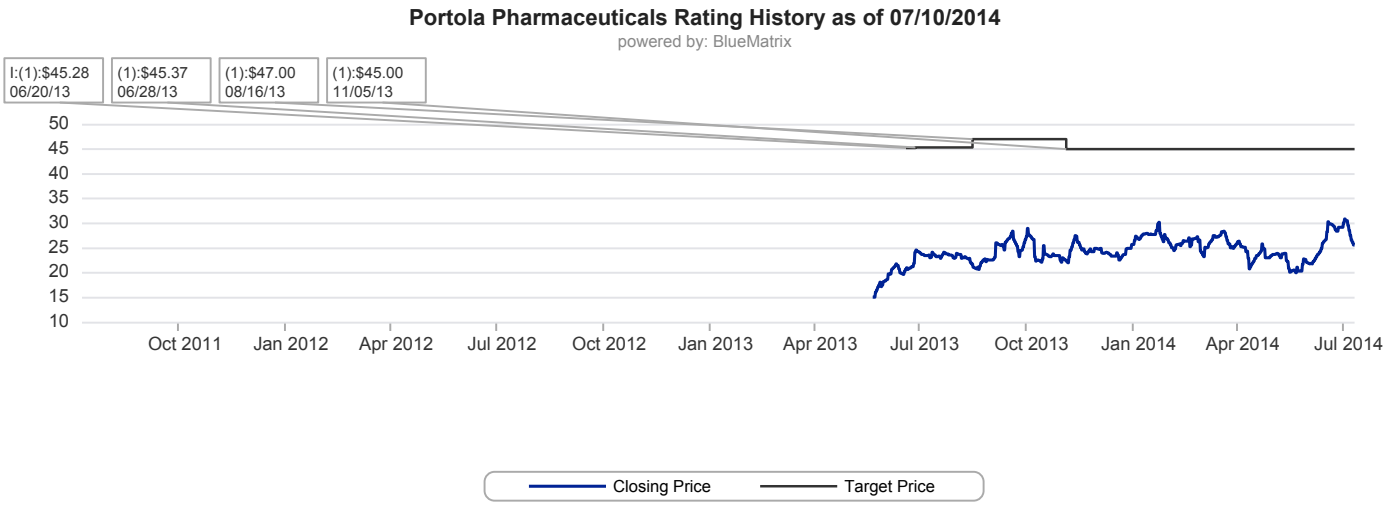

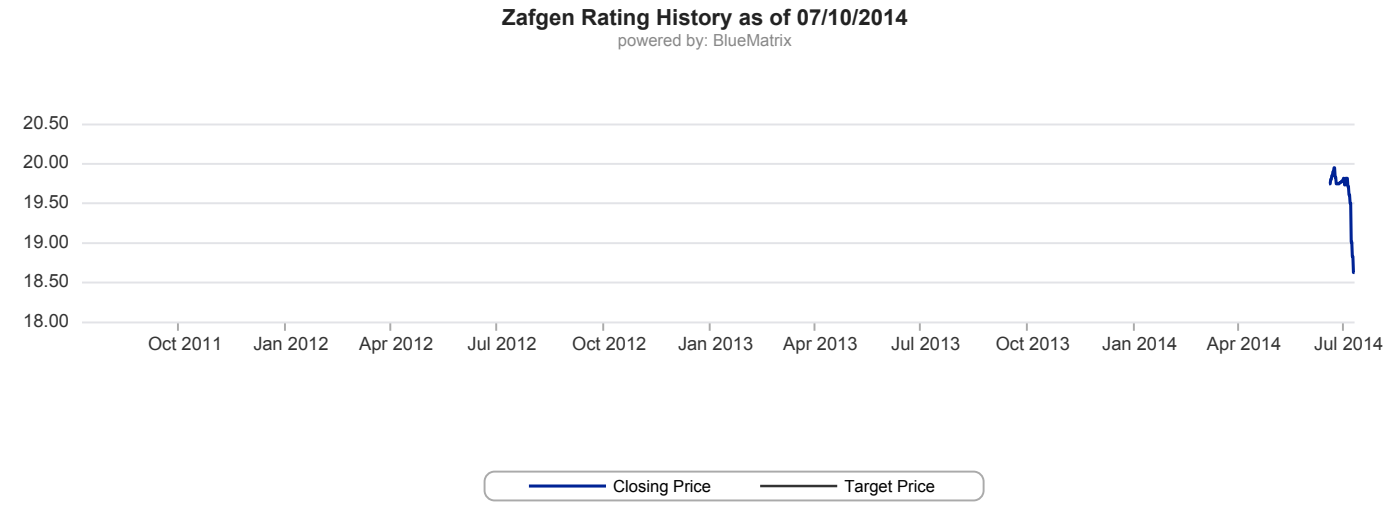

Legend for Price Chart:

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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