Zafgen, Inc. (ZFGN)

Initiating Coverage at Market Outperform; Novel Drug for Orphan Metabolic Diseases

MARKET DATA

Price	$18.84
52-Week Range:	$17.50 - $21.01
Shares Out. (M):	22.7
Market Cap ($M):	$427.7
Average Daily Vol. (000):	23.0
Cash (M):	$135
Cash/Share:	$5.95
Enterprise Value (M):	$295
LT Debt (M):	$0

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2013A	2014E	2015E
Revenue ($M)	1Q	$0.0	$0.3A	--
	2Q	$0.0	$0.0	--
	3Q	$0.0	$0.0	--
	4Q	$0.0	$0.0	--
	FY	**$0.0**	**$0.3**	**$0.0**
EPS	1Q	($4.94)	($5.82)A	--
	2Q	--	($8.37)	--
	3Q	--	($0.69)	--
	4Q	--	($0.75)	--
	FY	**($19.53)**	**($15.64)**	**($2.09)**

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE

MARKET OUTPERFORM | Price: $18.84 | Target Price: $31.00

INVESTMENT HIGHLIGHTS

We are initiating coverage on Zafgen, Inc. with a Market Outperform rating and $31 price target. Zafgen is a biopharmaceutical company focused on the development of treatments for orphan, obesity-related metabolic diseases. Its lead candidate is beloranib, a MetAP2 inhibitor for two indications: Prader-Willi Syndrome (PWS), a genetic disorder that renders patients morbidly obese, and craniopharyngioma-associated obesity (i.e., acquired PWS). Beloranib is entering Phase 3 trials in PWS, with results anticipated by YE15, and is undergoing a Phase 2 trial for craniopharyngioma-associated obesity, with results expected in 1Q15. Phase 1b/2a results have consistently shown potent weight loss efficacy, and other metabolic and behavioral improvements, providing us with confidence for the success of later-stage studies. Given the high, unmet medical need in these orphan indications, we view the commercial opportunity for beloranib as compelling. Zafgen completed its IPO on June 19, 2014 and we anticipate two late-stage clinical catalysts within a 12-month time horizon as key value drivers for the stock. Our $31 target is derived though a sum-of-the-parts NPV analysis of beloranib in PWS and in craniopharyngioma-associated obesity.

Phase 3 results for beloranib in PWS anticipated by YE2015; the key value-driving catalyst. Two Phase 3 trials for beloranib in PWS are slated to begin in 2H14 and 1Q15. Positive results from the trials could show significant improvement in total body fat mass and/or hyperphagia-related behaviors, with success in either acceptable for regulatory approval. Our confidence in positive Phase 3 results in based upon results from completed proof-of-concept trials including a 17-patient, Phase 2a trial in PWS patients. The trial showed that beloranib reduces body fat vs. placebo and improves hyperphagia-related behavior with a favorable safety profile. In our view, these results establish beloranib as having potential to be a viable treatment option for PWS patients.

Beloranib in craniopharyngioma-associated obesity; an additional value driver. Zafgen is also conducting a Phase 2a proof-of-concept trial in craniopharyngioma-associated obesity, with results expected in 1Q15. The trial will enroll 14 patients and include body weight, composition, and hunger as endpoints. In addition, Zafgen's pipeline includes second-generation MetAP2 inhibitors, including orally available candidates, with potential additional indications of severe obesity and NASH.

Commercial potential in orphan indications is attractive. While both PWS and craniopharyngioma-associated obesity are rare diseases, with estimated prevalence rates of up to 1:8,000 in the U.S., we believe the lack of viable treatment options and compelling proof-of-concept data for beloranib support that these indications are attractive commercial targets. We project that the drug candidate could be approved in the U.S. by YE2017 and achieve global peak sales in these two indications totaling ~ $870MM by the time the polymorph patents are expected to expire in 2031.

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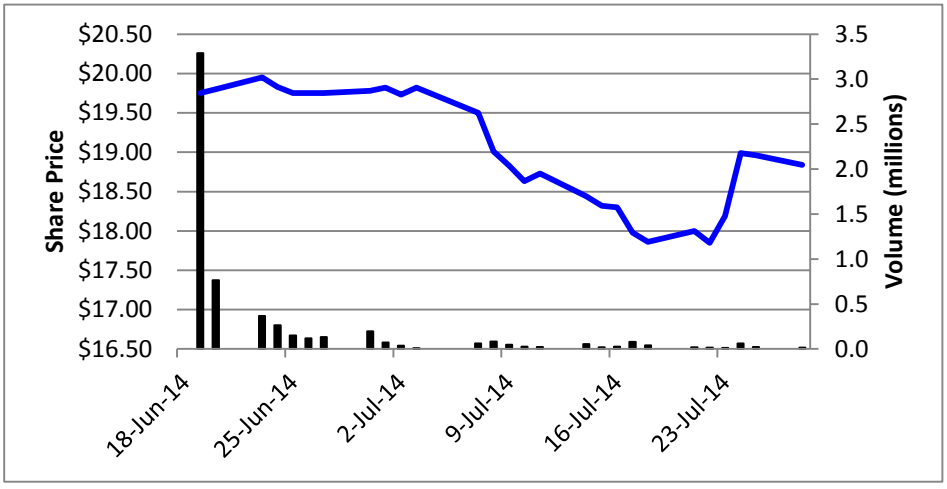
COMPANY DESCRIPTION

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

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

FIGURE 1. Zafgen Stock Chart



Source: Thomson Reuters

KEY UPCOMING MILESTONES

2H14	Beloranib	Initiate U.S. Phase 3 trial for Prader-Willi Syndrome
2H14	Beloranib	Initiate Phase 2b trial for severe obesity
1Q15	Beloranib	Phase 2a results in craniopharyngioma-associated obesity
1H15	Beloranib	Initiate European Phase 3 trial for Prader-Willi Syndrome
YE2015	Beloranib	Data from Phase 3 trial for Prader-Willi Syndrome

INVESTMENT THESIS

Focus on significant unmet medical needs in orphan metabolic diseases. Zafgen is focused on developing novel drugs to treat orphan metabolic diseases. Its lead candidate, beloranib, is a first-in-class MetAP2 inhibitor, in development for Prader-Willi Syndrome (PWS) and craniopharyngioma-associated obesity, both orphan disorders involving severe obesity, reduced quality of life and shortened life expectancy. PWS is a genetic, orphan designated disorder characterized by hyperphagia (or unrelenting hunger that renders patients morbidly obese) and prevalence is estimated at 1:8,000 to 1:50,000. Craniopharyngioma-related obesity (i.e., acquired PWS) results from the surgical removal of certain pituitary tumors and causes appetite and satiety deregulation similar to PWS. There are no approved treatments for these orphan conditions and current pharmacological and surgical weight loss treatments have not demonstrated benefit in these patients. We see a significant opportunity for a novel, safe and effective therapy that addresses both the physical and behavioral symptoms of these diseases.

Phase 3 program in PWS to begin in 2H14; Phase 2a results supportive of success. We expect Zafgen to initiate a U.S. Phase 3 trial for beloranib in PWS patients in 2H14, with results anticipated by YE2015. A second trial, in Europe, is expected to begin in 1H15. We believe positive results from these two trials can support regulatory approvals in both geographies and we view them as the primary value-driving catalysts for the stock. In our view, the probability of successful Phase 3 results in PWS is high based on the results demonstrated for beloranib in Phase 1b and Phase 2a trials to date. These trials have consistently demonstrated dose-dependent and potent weight loss efficacy and reductions in body fat content. Furthermore, in a 14-patient, proof-of-concept Phase 2a trial in PWS patients, not only did treatment with beloranib result in statistically significant weight loss at four weeks, but clear benefits were observed for hyperphagia-related behaviors. In our view, the improvements in hyperphagia-related behaviors are especially compelling and, if supported by the Phase 3 trials, would represent an important driver of adoption for the drug in this patient population.

Phase 2 trials advancing in additional indications. In addition to the Phase 3 program in PWS patients, Zafgen is currently conducting a Phase 2a proof-of-concept trial for beloranib in patients with craniopharyngioma-associated obesity. Results from this trial are anticipated in 1Q15 and represent a meaningful value driver for the stock, in our view. Based on similarities between PWS and craniopharyngioma-associated obesity, and the consistently positive clinical results generated for beloranib so far, we are also confident in positive results from this trial, which we believe would support rapid advancement into a pivotal program. Also, the company intends to initiate a Phase 2b trial for beloranib in patients with severe obesity in 2H14. We see this broader market opportunity as attractive, in particular for follow-on, orally available formulations the company is developing. Furthermore, we note that initial studies support a more efficacious weight loss profile (up to ~10.5% placebo-adjusted weight loss at 12 weeks) than recently approved and late-stage development obesity drugs.

Commercial opportunity for beloranib in orphan indications is attractive. We project peak sales for beloranib in PWS and craniopharyngioma-associated obesity approaching $900MM (U.S. and Europe), which we believe reflects conservative assumptions for the size of the addressable patient population. We view the product candidate's intellectual property as strong, with polymorph compositions of matter patents expected to provide protection through 2031. We expect the product to

receive standard orphan drug exclusivity, providing further confidence in market protection. Zafgen is also developing ZGN-839, a second generation MetAP2 inhibitor with oral bioavailability. The drug candidate has demonstrated efficacy in animal models of NASH, fibrosis, and Type 2 diabetes. We estimate that it could be ready to enter clinical development in 2015. This program, if successful, can allow Zafgen to leverage its product into several indications, potentially adding value to the pipeline not accounted for in our current valuation assumptions.

Experienced leadership team with strong balance sheet following successfully completed IPO. Zafgen has assembled a management team with extensive expertise in the cardiometabolic space. CEO Thomas Hughes, Ph.D., led the Cardiovascular and Metabolic Diseases therapeutic area at the Novartis Institutes for BioMedical Research in Cambridge, MA. The company's newly appointed President, Patrick Loustau, was the Senior Vice President for Global Commercialization (Cardiovascular & Metabolics) at Bristol-Myers Squibb and previously held management positions at Novo Nordisk. Also, CMO Dr. Dennis Kim has extensive experience in obesity clinical development, including at Orexigen Therapeutics (OREX, MO, $12 PT) and Amylin Pharmaceuticals. Zafgen completed its IPO last month, raising sufficient funds to complete planned clinical trials in lead orphan indications and severe obesity, which we view as significant value-driving catalysts for the company.

VALUATION

We value Zafgen based on our projections for beloranib sales in PWS and craniopharyngioma-related obesity. As summarized in Figure 2, our $31 price target is derived through a sum-of-the-parts NPV valuation that includes sales of the drug for each of these two orphan indications in the U.S. and Europe. Our revenue projections are described in detail on page 22. Our NPV analyses assume market exclusivity through 2031, when the issued U.S. polymorph patent for beloranib expires (and when the pending European patent application is expected to expire). We assume a 75% probability of success for PWS and 60% probability of success in craniopharyngioma-related obesity, based on available Phase1b/2a data. We also ascribe a 12.5% discount rate to reflect cost of capital. Our $31 price target also includes our projection for YE2014 cash of ~$103MM, or $4.55 per share.

FIGURE 2. Zafgen Sum-of-the-Parts NPV Valuation

	Peak revenue (MM)	Peak revenue year	Economics	Probability of success	Discount rate	NPV	NPV per share	Contribution
Beloranib- PWS	**469.3**	**2030**	**100%**	**75%**	**12.5%**	**364.4**	**$16.05**	**52%**
U.S	346.5	2030	100%	75%	12.5%			
Europe	122.9	2030	100%	75%	12.5%			
Beloranib-Cranio	**400.0**	**2030**	**100%**	**60%**	**12.5%**	**234.4**	**$10.32**	**33%**
U.S	277.2	2030	100%	60%	12.5%			
Europe	122.9	2030	100%	60%	12.5%			
Cash (YE14)						**103.3**	**$4.55**	**15%**
Price target							**$30.92**	**100%**

Source: JMP Securities LLC and Company Reports

Capital Structure

Following the completion of the company's IPO, Zafgen had approximately 22.7 million shares outstanding, including full exercise of the over-allotment option. There are a further ~1.5 million stock options outstanding and ~2.5 million shares reserved for issuance under stock option and incentive plans.

Balance Sheet

As of March 31, 2014, the company had cash and cash equivalents of ~$39MM. Net proceeds from the IPO, including full exercise of the over-allotment option were ~$103MM. We believe Zafgen should have enough cash, proceeds, and credit to fund operations into 2017, including the completion of the ongoing and planned trials for beloranib in PWS, craniopharyngioma-related obesity, the development of the drug in severe obesity in the general population, and investing in pipeline assets (second generation MetAP2 inhibitors). We assume the company will need to raise additional cash to fund the launch of the drug; however, we anticipate multiple value-driving catalysts ahead of this.

INVESTMENT RISKS

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

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

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

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

HIGH UNMET MEDICAL NEED IN ORPHAN DISORDERS OF FAT METABOLISM

Prader-Willi Syndrome (PWS)

Prader-Willi Syndrome (PWS) is a rare genetic disorder characterized by physiologic and behavioral symptoms, including hyperphagia (excessive hunger) and obesity. The condition is caused by a deletion or unexpression of genes in the 15th chromosome. This genetic abnormality causes dysfunction or impairment of the hypothalamus, the area of the brain that regulates metabolism and appetite. Extreme and insatiable hunger, known as hyperphagia, and overeating behavior can lead to severe, life-threatening obesity. Other symptoms include hypotonia, neuro-cognitive, behavioral, ophthalmic, and endocrine issues.

The incidence of PWS is estimated to range between 1 in 8,000 and 1 in 50,000 live births in the U.S. and Europe. PWS patients are subject to premature death from choking, stomach rupture, or tissue necrosis, or from complications caused by morbid obesity, including heart failure and respiratory failure. The average life expectancy of PWS patients is ~32 years of age. There are no effective pharmacological treatments for patients with PWS and bariatric surgery is contraindicated in these patients due to poor outcomes and serious complications, such as rupture of the stomach or esophagus that can be life threatening.

Current treatments for PWS patients

In addition to speech and occupational therapy, children with PWS are treated with recombinant growth hormone to increase height, muscle mass, and reduce fat mass. Although some weight-loss drugs are likely used off-label, there is no FDA-approved pharmacological treatment specific to PWS on the market. We believe beloranib could be used as adjunct therapy along with the aforementioned treatments. In January 2013, the FDA granted orphan drug designation for beloranib in PWS. Zafgen is eligible for orphan drug exclusivity in the U.S., which would allow the company to be the sole marketers of the drug for several years. We note that on July 10, 2014, the EU granted orphan drug designation for beloranib in PWS.

Craniopharyngioma-Associated Obesity

Craniopharyngioma is a brain tumor originating from the pituitary gland, with a prevalence of 1:50,000, commonly seen in children, but it may also affect older adults. The tumor is slow-growing and benign; however, its location in the brain can affect the immune and endocrine systems. Symptoms can include short stature, polyuria, vision loss, fever, and/or a balance disorder among others. Treatment involves excision of the tumor by neurosurgery that can lead to complications, including damage to the patient's feeding control centers, resulting in morbid obesity for approximately 50% of patients. Due to the PWS-like insatiable hunger and reduced metabolic rate, the condition is sometimes referred to as "acquired PWS". As in PWS, the condition reduces quality of life and there is no pharmacological treatment available for these patients.

BELORANIB – A FIRST-IN-CLASS METAP2 INHIBITOR

Zafgen is focused on the development of MetAP2 (methionine aminopeptidase) inhibitors for the treatment of obesity and obesity-related conditions. MetAP2 is an enzyme involved in the modulation of key cellular processes that control metabolism. It is a novel therapeutic target that has been demonstrated to be associated with reducing hunger and rebalancing fat metabolism. Its unique mechanism of action includes stimulating the use of stored fat as an energy source, and addressing dysregulation of fat metabolism in an obese subject, which causes more fat to be made and stored than in a lean person. While the exact mechanism of action is unknown, it is thought to include effecting changes in ERK phosphorylation, the cellular stress cascade, gene expression, metabolites, and hormones (FGF-21, adiponectin).

The company's lead clinical development candidate is beloranib, a first-in-class, injectable, MetAP2 inhibitor. The compound is a structural analog of fumagillin, initially used as an antimicrobial agent and has been investigated as a cancer therapeutic due to its anti-angiogenic properties. MetAP2 inhibitors, including beloranib, have been shown to be associated with weight loss in animal models where both increased fat oxidation and reduced food intake were observed. In preclinical studies, beloranib was demonstrated to be a potent MetAP2 inhibitor that acts through the liver and adipose tissue to rebalance lipid metabolism and reduce hunger.

FIGURE 3. MetAP2 Inhibitor Mechanism of Action

Source: Company reports

Toxicology studies have been completed in beagle dogs, rats and rabbits, including long-term studies in rats (six-month duration) and dogs (nine-month duration), the results of which have been submitted to the FDA for review. Based on the safety findings in animals, clinical trials of beloranib have included monitoring for blood cell changes, sperm counts and sperm morphology, and frequent pregnancy testing and requirements for birth control in women. We view the pre-clinical safety profile of the drug as favorable.

BELORANIB CLINICAL DEVELOPMENT PROGRAM

The development of beloranib is focused on two orphan indications that involve severe obesity, reduced quality of life, and shortened life expectancy: Prader-Willi Syndrome (PWS) and craniopharyngioma-associated obesity. The company has conducted five proof-of-concept studies evaluating beloranib in over 200 patients, including Phase 2a trials in PWS and general obesity. Results from these studies have consistently demonstrated potent weight loss efficacy with beloranib as well as improvements in other metabolic risk factors (reductions in levels of low density lipoprotein cholesterol (LDL-C), C-reactive protein (CRP) and systolic blood pressure), and important hyperphagia-related behavioral benefits in PWS patients.

The company has completed an end-of-Phase 2 meeting with the FDA and is currently finalizing pivotal protocol designs with U.S. and European regulatory agencies, before advancing into Phase 3 trials for beloranib in PWS in the U.S. in 2H14, and in the EU in 1H15. Additionally, the company has initiated a Phase 2 trial in craniopharyngioma-associated obesity and plans to start a Phase 2 trial in severe obesity in the general population in 2H14.

FIGURE 4. Zafgen Pipeline

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

Source: Company reports

In addition to the development of beloranib, Zafgen also has second-generation MetAP2 inhibitors in preclinical development for severe obesity and ZGN-839, another MetAP2 inhibitor, in preclinical development for NASH (non-alcoholic steatohepatitis), non-alcoholic fatty liver disease, abdominal obesity, and Type 2 diabetes. The company intends to enter into development partnerships for these product candidates. We anticipate INDs to be filed by 1H15. As these candidates flow through Zafgen's pipeline, they should add value to the company, in our opinion.

Pivotal Phase 3 program for PWS to initiate in 2H14

Based on positive Phase 2 results, and discussions with U.S. and European regulatory agencies, Zafgen plans to advance beloranib into a pivotal development program in PWS beginning in 2H14. We expect the first Phase 3 trial will initiate enrollment of patients in the U.S. in 2H14 (ZAF-311, NCT02179151), with top-line results anticipated by YE15. A second, European-based trial is planned to begin in 1H15.

Both of these Phase 3 trials are planned to be randomized, double-blind, placebo-controlled studies. The final protocol agreement with regulatory agencies is pending; however, we expect the trials to assess the efficacy, safety, and tolerability of two doses of beloranib (1.8mg and 2.4mg) versus placebo over an initial, double-blinded treatment period of six months, likely followed by an additional six-month, open-label treatment period. Target enrollment for the trials in total is ~240 patients, 12 years of age or older with a BMI >30kg/m^2, in at least ten sites in the U.S. and EU, respectively.

The primary endpoints of the Phase 3 trials will be total body fat mass (% change from baseline as measured by DEXA) and hyperphagia-related behavior (as measured by PWS-HQ), with success in either as acceptable for regulatory approval. Secondary endpoints include body weight, LDL-C, HDL-C, C-reactive protein, skin-picking behavior, and quality of life.

We view the Phase 3 program in PWS as the key value driver for Zafgen. A positive result could show a significant improvement in total body fat mass and/or hyperphagia-related behaviors. Its unique mechanism of action appears to reduce weight by a higher percentage than obesity drugs on the market, such as phentermine, Belviq, and Qsymia. If so, beloranib would have the potential to be the first FDA-approved, oral, PWS treatment in the market. In our view, positive Phase 3 results in this orphan indication with a high unmet need would support rapid adoption and chronic treatment.

Additional Phase 2 trials planned in craniopharyngioma-associated obesity and severe obesity

Zafgen has also initiated a Phase 2a trial in craniopharyngioma-associated obesity (ZAF-221, NCT02063295) and results are expected in 1Q15. Similar to PWS, craniopharyngioma-associated obesity is caused by dysregulation of the hypothalamus and is often referred to as “acquired PWS”. As such, although this is the first trial being conducted with beloranib in this patient population, we believe there is strong rationale for success. The Phase 2a trial is a randomized, double-blind, placebo-controlled study designed to enroll 14 patients with radiographically confirmed hypothalamic damage. Patients are being randomized to receive treatment with beloranib (1.8mg) or placebo for four weeks. The primary endpoint for this trial is change in body weight and additional endpoints include metabolic risk markers (cholesterol, triglycerides, CRP), assessments of hunger, and quality of life.

In addition, the company is planning to initiate a Phase 2b trial in patients with severe obesity in 2H14. The trial is intended to build upon the clinical data set already generated in the general obesity population and evaluate beloranib in patients with Type 2 diabetes who are also severely obese (BMI 30-60 kg/m^2). The trial is planned to assess treatment over an initial six-month period, with results expected in 4Q15, and a further six months follow-up.

Phase 1/2 results establish proof of concept and inform late-stage development plans

As summarized below (Figure 5), Zafgen has completed three Phase 1b trials and two Phase 2a trials for beloranib The results of these trials consistently established dose-dependent weight loss efficacy, as well as metabolic benefits and a reduction in hyperphagia-related behaviors in PWS patients. Additionally, we believe these studies enabled optimal dose selection, maximizing the potential for therapeutic benefit with a favorable safety and tolerability profile.

FIGURE 5. Summary of Beloranib Phase 1b and Phase 2a Trials and Results

Trial	Trial description	Observations
Phase 1b		
ZAF-001	• Randomized, double-blind, placebo controlled trial • Escalating doses of 0.1mg/m2, 0.3mg/m2, and 0.9mg/m2, • 1-hour intravenous infusion twice weekly • 4 weeks treatment duration • BMI range 32-45 kg/m2	• Dose dependent weight reductions • Dose depended metabolic benefits • Safe and well tolerated at all dose levels
ZAF-003	• Randomized, double-blind, placebo controlled trial • Static dosing scheme of 3.0mg, 6.0mg, and 2.5mg • 1-hour intravenous infusion • Once-weekly and twice-weekly dosing regimens • 4 or 7 weeks treatment duration • BMI range 30-50 kg/m2	• Dose dependent weight reductions • Once-weekly regimen less effective than twice-weekly administration • Doses of 3.0mg or lower were well tolerated and effective • 6.0mg not very well tolerated (gastrointestinal side effects and sleep disturbance)
ZAF-101	• Randomized, double-blind, placebo controlled trial • 1.0mg, 2.0mg, and 4.0mg were evaluated • Subcutaneous injection twice weekly • 4 weeks treatment duration • BMI range 30-45 kg/m2	• Significant weight reduction with all doses • Metabolic benefits and sense of hunger reduced with all doses • 4.0mg not very well tolerated (gastrointestinal side effects and sleep disturbance)
Phase 2a		
ZAF-201	• Randomized, double-blind, placebo controlled trial • Parallel design trial • Fixed beloranib doses (0.3mg, 0.6mg, 1.2mg, 2.4mg, 3.2mg) • Subcutaneous injections twice-weekly • 12 weeks treatment duration • BMI range 30-50 kg/m2	• 0.3mg not effective, 3.2mg not well tolerated • Progressive and dose dependent weight reduction • Comparable metabolic and body composition benefits observed as with prior studies • Most adverse events, including sleep disturbances, mild-moderate and transient
ZAF-211	• Enrolled patients with Prader-Willi Syndrome • Randomized, double-blind, placebo controlled trial • 1.2mg and 1.8mg doses of beloranib evaluated • Subcutaneous injections twice-weekly • 4 weeks treatment duration • BMI range 26-44 kg/m2	• Trend toward reduction in body weight • Reduction in body mass assessed by DEXA • Reduction in total fat mass assessed by DEXA • Reduction in hyperphagia related behaviors at 1.8mg dose

Source: Company reports

Phase 1b trials

Zafgen conducted three Phase 1b trials to assess the pharmacokinetics, safety, and tolerability of beloranib. These trials established the optimal dose of intravenously administered beloranib to be between 0.65mg and 3mg. In all trials, dose-dependent weight loss efficacy was observed along with improvements in other metabolic markers.

ZAF-001 (NCT01028261) was a four-week, escalating dose (0.1mg/m^2, 0.3 mg/m^2, and 0.9 mg/m^2) trial of beloranib administered in a one-hour IV infusion twice a week. The BMI of patients ranged from 32-45 kg/m2. Results showed dose-dependent weight reduction and metabolic benefits, with weight loss at the highest dose (0.9 mg/m^2) of 3.6kg, compared to the placebo weight loss of 1.2kg (Figure 6). All doses were safe and well-tolerated.

FIGURE 6. Key Results: ZAF-001 Phase 1b, Four-week Trial of IV Beloranib

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)	p-value*
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	—

* statistical analysis was not performed in this proof of concept trial

Source: Company reports

ZAF-003 (NCT01372761) was a four- or seven-week, static-dose trial of 3.0mg, 6.0mg, and 2.5 mg, in n=25, obese females of non-childbearing potential. The BMI of patients ranged from 30-50 kg/m2. One-hour intravenous infusion of 3.0mg and 6.0mg doses was given twice weekly for four weeks, or a 2.5mg dose was given twice weekly for the first week and once-a-week for the subsequent six weeks. Results showed dose-dependent weight reduction with the twice-weekly regimen more efficacious than the once-a-week regimen (Figure 7). The highest dose, 6.0mg, was not well tolerated with dose-limiting adverse events seen, including gastrointestinal side effects and sleep disturbances. Doses of 3.0 mg or lower, however, were well tolerated and effective.

FIGURE 7. Key Results: ZAF-003 Phase 1b, Four-week Trial of IV Beloranib

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)	p-value*
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	—

* statistical analysis was not performed in this proof of concept trial

Source: Company reports

ZAF-101 (NCT01507077) was a four-week, randomized, double-blind trial evaluating beloranib administered via a subcutaneous injection twice a week. This was the first trial where beloranib was administered via subcutaneous injection vs. intravenous infusion in previous Phase 1b trials. The BMI of patients ranged from 30-45 kg/m^2. The trial evaluated the following doses of the drug: 1.0mg, 2.0mg, and 4mg. The study showed significant weight reduction with all doses along with metabolic benefits including a reduction in the sense of hunger (Figure 8). Adverse events such as gastrointestinal side effects and sleep disturbances were seen in the 4.0mg dose.

FIGURE 8. Key Results: ZAF-101 Phase 1b, Four-week Trial of SC Beloranib

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: Company reports

Phase 2a trial in obese patients

The first Phase 2a trial Zafgen conducted with beloranib was in severely obese patients (ZAF-201, NCT01666691). Consistent with the ZAF-101 trial, beloranib was administered via subcutaneous injection in this trial. The results from this trial demonstrated statistically significant weight loss efficacy, as well as improvements in markers of cardiometabolic risk.

ZAF-201 was a randomized, double-blind, placebo-controlled, parallel dose study conducted at eight clinical centers in Australia. The trial enrolled 160 obese patients with a BMI of 30-54 kg/m^2, with or without Type 2 diabetes. Patients were randomized to receive one of a range of fixed beloranib doses (0.3mg, 0.6mg, 1.2mg, 2.4mg, and 3.2mg), or placebo, twice weekly over a 12-week, double-blind period. The average age of patients was 48.4 years with a BMI range of 30-54 kg/m^2. Key efficacy endpoints assessed included weight loss and changes in body composition as measured by bio-impedence, and pharmacokinetic/pharmacodynamic parameters. Safety and tolerability were also evaluated.

Results from this trial showed that beloranib doses ranging from 0.6mg to 2.4mg resulted in dose-related weight loss (Figure 9). The highest dose, 2.4mg, was associated with the most significant and rapid onset of weight loss, however, it was less well-tolerated and was eliminated from the study within the first four weeks. The lowest dose, 0.3mg, was also eliminated from the trial due to poor efficacy. Metabolic and body composition benefits were consistent with those demonstrated in earlier trials.

FIGURE 9. ZAF-201 Phase 2a Trial Shows Dose-Related Weight Loss

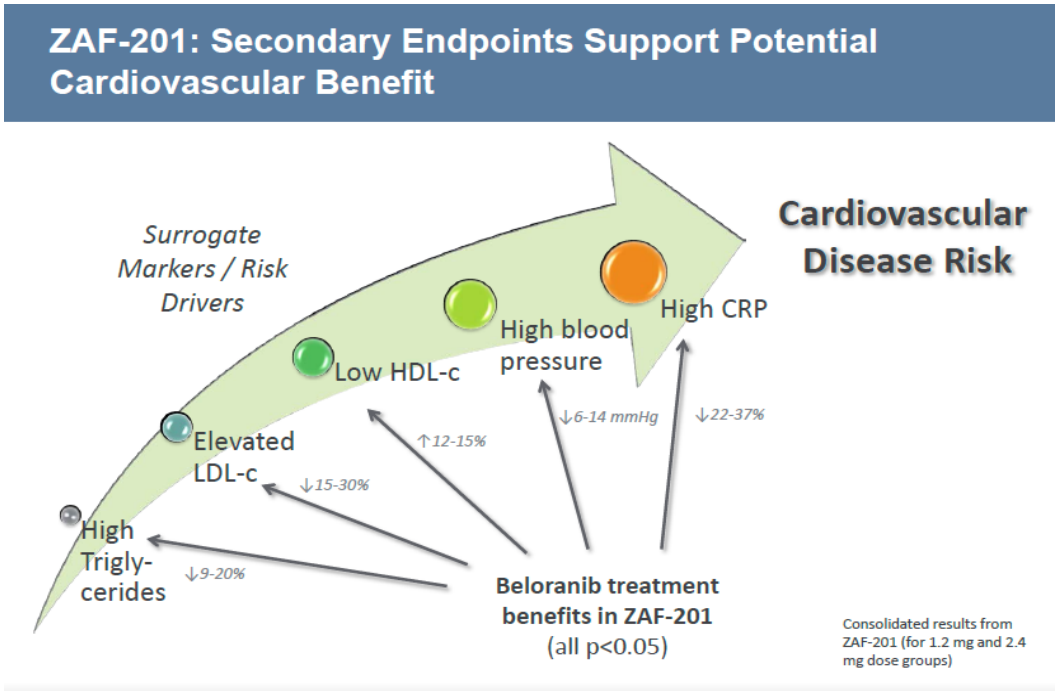
12-week Phase 2a Proof of Concept Clinical Trial in Obese Patients (ZAF-201)

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: Company reports

Zafgen decided to measure systemic biomarkers of cardiovascular disease risk, due to a higher risk in obese patients, including LDL cholesterol, HDL, CRP, and triglycerides. Results suggest that beloranib treatment does not increase the risk of cardiovascular disease (Figure 10). There were no deaths or SAE (severe adverse events). TEAEs (treatment-emergent adverse events), such as sleep disturbances, were generally mild in severity and transient.

FIGURE 10. ZAF-201 Beloranib Does Not Increase Cardiovascular Risk



Source: Company reports

Zafgen plans to conduct a Phase 2b study of beloranib in severe obesity, in diabetic patients with a BMI up to 60 kg/m2, to demonstrate sustained 6-12 month weight loss. The company plans to initiate the study in 2H14 and initial six-month data is expected in 4Q15. In addition, Zafgen is also considering developing a second-generation MetAP21 candidate for severe obesity.

Phase 2a trial in PWS patients

ZAF-211 (NCT01818921) was a four-week, Phase 2a proof-of-concept trial enrolling 17 PWS patients. It was a placebo-controlled, double-blinded trial evaluating safety and tolerability and the effects of 1.2mg or 1.8mg doses of beloranib on body weight, body composition, and hyperphagia-related behaviors. Results showed a reduction in fat mass and total body mass despite an increase in calorie intake (Figures 11 &12).

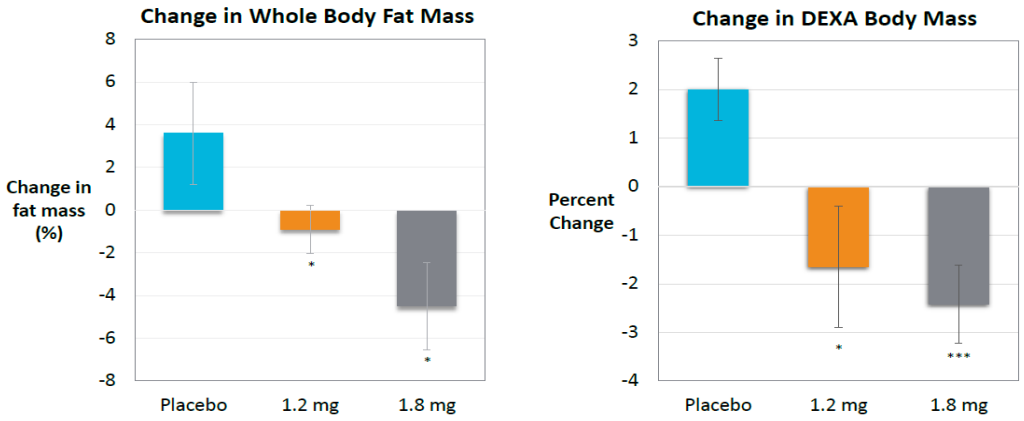
FIGURE 11. Key Results: ZAF-211 Phase 2b Four-week Trial of Beloranib

Four-Week Phase 2a Proof of Concept Clinical Trial in Patients with Prader-Willi Syndrome (ZAF-211)

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: Company reports

FIGURE 12. ZAF-211 Fat Mass, Total Body Mass Reduction Despite Increased Calories



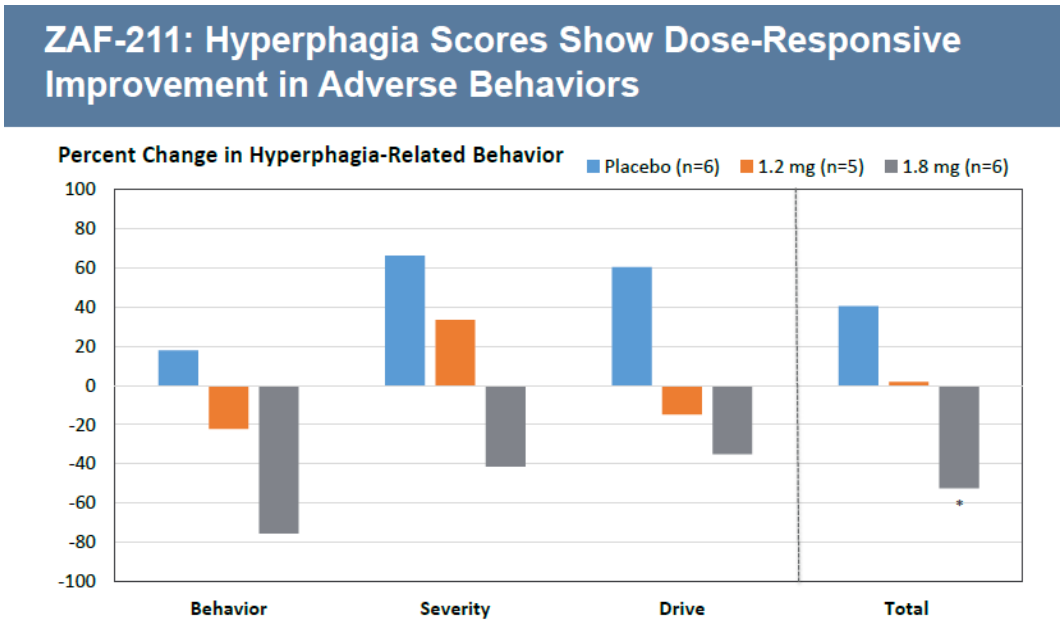
*, p<0.05; ***, p<0.005
Body composition and mass assessed by DEXA, dual-energy X-ray absorptiometry

Source: Company reports

During the course of the trial, including a two-week, placebo run-in phase, daily calorie allowances were increased in all patients by 50% to drive modest weight gain. Results were as follows. Levels of HDL cholesterol were increased by an average of 26% in beloranib-treated patients, compared to an average increase of 1% in patients dosed with placebo (p=0.005). Levels of LDL cholesterol were reduced by an average of 27% in beloranib-treated patients, compared to an average increase of 3% in patients dosed with placebo (p=0.005).

Hyperphagia-related behaviors typical of PWS patients were reduced by an average of 52.4% by treatment with a 1.8mg dose of beloranib, compared to an average increase of 40.5% in patients dosed with placebo and an average increase of 1.8% in patients treated with 1.2mg beloranib (Figure 13).

FIGURE 13. ZAF-211 Trial Shows Dose-Related Reduction in Hyperphagia



Source: Company reports

The change in behavior was statistically significant from baseline for patients treated with the 1.8 mg dose of beloranib (not statistically significant by ANCOVA; p=0.025 by post hoc paired t-test). No adverse events were seen in the trial.

The study confirmed a clear drug pathway for beloranib in PWS and established the registration endpoints to be used in the Phase 3 trials as improvement in hyperphagia-related behavior and reduced body fat versus placebo. In this trial, beloranib was well-tolerated and no safety signals were seen.

BELORANIB COMMERCIAL OPPORTUNITY AND REVENUE MODEL

We model beloranib sales in the U.S. and Europe in both the PWS and craniopharyngioma-associated obesity. Together, we believe that these markets represent an ~$900MM opportunity for beloranib, as detailed below.

Prader-Willi Syndrome (PWS)

Estimates for the prevalence of PWS range from 1:8,000 to 1:50,000. For the purpose of our revenue projections, we use the most conservative end of this range, 1:50,000, and estimate a prevalence in the U.S. of just over 6,500 patients and roughly the same number of patients in Europe (EU5). We estimate that 50% of these patients are over 12 years of age and are eligible for treatment (based on anticipated inclusion criteria of the Phase 3 trials). We assume that beloranib is approved for the treatment of PWS and launched in the U.S. in 2017 and approximately one year later in Europe, and project that at peak (fifth full year of launch) the drug can achieve a 50% market penetration. This market share assumption reflects both the positive data observed for beloranib, to date, and the high unmet medical need of PWS patients. Finally, we assume a price of treatment of $120,000 per year in the U.S. and annual price increases of 5%, and a gross-to-net adjustment of 15%. In Europe, we assume an annual cost of $80,000 with no price increases. Based on these assumptions (summarized in Figure 14), we project peak sales of beloranib in the U.S. approaching $370MM when the polymorph patents expire in 2031, and ~$125MM in Europe.

Craniopharyngioma-associated obesity

It is estimated that the annual incidence of craniopharyngioma is 0.13 to 0.17 per 100,000, or approximately 400-500 new cases per year in the U.S. In addition, patients with craniopharyngioma-associated obesity may have a longer life expectancy than PWS patients. Consistent with our assumptions for PWS, we include the most conservative estimate in our model, representing a prevalence of 1:50,000. We assume that beloranib is approved for the treatment of PWS and launched in the U.S. in 2018 and approximately one year later in Europe. Our modeled penetration rates in craniopharyngioma patients are lower than those for PWS, peaking at 20%, reflecting some uncertainty on the number of patients who develop craniopharyngioma-associated obesity. Again, using a treatment cost per year of $120,000 in the U.S. and $80,000 in Europe, we project peak sales of beloranib of ~$295MM and $125MM in 2031, respectively in these geographies (see Figure 15).

Commercial infrastructure

We expect Zafgen to commercialize beloranib through its own sales force in the U.S. and Europe. The initial indications for the drug are orphan and we believe there is a concentrated prescriber base that is well-suited to a small specialty sales infrastructure.

Intellectual property

Zafgen owns rights to patents and patent applications covering beloranib compositions of matter, formulations, polymorphs, methods of treating obesity using dosing regimens of beloranib, and methods of treating hypothalamic obesity. We expect the issued patents to provide protection through at least 2031, which is the year through which we project sales for our NPV analyses. We do not assume any terminal value for beloranib after 2031.

There are issued composition of matter patents in the U.S. and Europe that will expire in 2019 and, importantly, two issued U.S. patents relating to beloranib polymorph compositions of matter that will expire in 2031. Additionally, there are two issued U.S. patents covering methods of treating obesity that will expire in 2029. In Europe, in addition to the issued composition of matter patent, the company has pending patent expirations covering polymorph composition of matter and methods of treating obesity that, once issued, would expire in 2031.

The company also owns two pending U.S. patent applications for the second-generation MetAP2 inhibitor program, with pending ex-U.S. counterpart patent applications and additional pending second-generation compound patent applications.

CKD license agreement

Our model includes royalties owed to licensors of beloranib and related patents. These royalties are reflected in the cost of goods sold and total mid-to-high single digit percentages of global net beloranib sales.

Zafgen in-licensed worldwide rights (excluding South Korea) to beloranib from Chong Kun Dang Pharmaceutical Corp. (CKD) in July 2009. The company paid an upfront license fee and agreed to make milestone payments of up to $30MM of which $1MM has been paid. In addition, CKD is entitled to receive a portion of sublicensing income and single-digit royalties based on annual net sales of beloranib. Zafgen has also exclusively licensed certain worldwide intellectual property rights to beloranib from the Children's Medical Center Corp., based on which Children's is entitled to receive single-digit royalties on beloranib sales until the covered patents expire.

Potential drivers of upside to our assumptions

We believe that our beloranib revenue projections could prove conservative for multiple reasons. Firstly, our pricing and penetration assumptions may prove conservative depending upon the strength of Phase 3 results, in our view, particularly relative to the on hyperphagia-associated behaviors and hunger. We also reiterate that our prevalence assumptions reflect the most conservative published estimates and the addressable patient populations may be more than five-fold larger than our assumptions. Lastly, we conservatively do not include in our model the use of beloranib in additional indications or geographies outside of the U.S. and Europe.

FIGURE 14. Beloranib Revenue Model – Prader-Willi Syndrome

U.S. revenue estimates	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**2031**
U.S. population	326,918,884	329,370,776	331,841,057	334,329,865	336,837,339	339,363,619	341,908,846	344,473,162	347,056,711	349,659,636	352,282,083	354,924,199	357,586,131	360,268,027	362,970,037
Population growth	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%
PWS prevalence	6,538	6,587	6,637	6,687	6,737	6,787	6,838	6,889	6,941	6,993	7,046	7,098	7,152	7,205	7,259
% PWS prevalence	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%
PWS patients (>12 years old)	3,269	3,294	3,318	3,343	3,368	3,394	3,419	3,445	3,471	3,497	3,523	3,549	3,576	3,603	3,630
% PWS patients >12 years	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Beloranib treated PWS patients	65	329	664	1,003	1,347	1,697	1,710	1,722	1,735	1,748	1,761	1,775	1,788	1,801	1,815
% penetration	2%	10%	20%	30%	40%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Annual cost of therapy	120,000	126,000	132,300	138,915	145,861	153,154	160,811	168,852	177,295	186,159	195,467	205,241	215,503	226,278	237,592
% price increase		5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
Gross U.S. beloranib sales ($MM)	**7.8**	**41.5**	**87.8**	**139.3**	**196.5**	**259.9**	**274.9**	**290.8**	**307.7**	**325.5**	**344.3**	**364.2**	**385.3**	**407.6**	**431.2**
Gross to net adjustment	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
Net U.S. beloranib sales ($MM)	**6.7**	**35.3**	**74.6**	**118.4**	**167.0**	**220.9**	**233.7**	**247.2**	**261.5**	**276.6**	**292.7**	**309.6**	**327.5**	**346.5**	**366.5**

EU revenue estimates	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**2025**	**2026**	**2027**	**2028**	**2029**	**2030**	**2031**
EU population	327,889,391	330,348,561	332,826,175	335,322,372	337,837,289	340,371,069	342,923,852	345,495,781	348,086,999	350,697,652	353,327,884	355,977,843	358,647,677	361,337,535	364,047,566
Population growth	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%
PWS prevalence	6,558	6,607	6,657	6,706	6,757	6,807	6,858	6,910	6,962	7,014	7,067	7,120	7,173	7,227	7,281
% PWS prevalence	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%
PWS patients (>12 years old)	3,279	3,303	3,328	3,353	3,378	3,404	3,429	3,455	3,481	3,507	3,533	3,560	3,586	3,613	3,640
% PWS patients >12 years	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Beloranib treated PWS patients		165	333	671	1,014	1,361	1,715	1,727	1,740	1,753	1,767	1,780	1,793	1,807	1,820
% penetration		5%	10%	20%	30%	40%	50%	50%	50%	50%	50%	50%	50%	50%	50%
Annual cost of therapy		80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000
% price increase		0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Gross U.S. beloranib sales ($MM)	**0.0**	**13.2**	**26.6**	**53.7**	**81.1**	**108.9**	**137.2**	**138.2**	**139.2**	**140.3**	**141.3**	**142.4**	**143.5**	**144.5**	**145.6**
Gross to net adjustment	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
Net U.S. beloranib sales ($MM)	**0.0**	**11.2**	**22.6**	**45.6**	**68.9**	**92.6**	**116.6**	**117.5**	**118.3**	**119.2**	**120.1**	**121.0**	**121.9**	**122.9**	**123.8**

Source: JMP Securities LLC and Company Reports

FIGURE 15. Beloranib Revenue Model – Craniopharyngioma-associated Obesity

U.S. revenue estimates	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
U.S. population	326,918,884	329,370,776	331,841,057	334,329,865	336,837,339	339,363,619	341,908,846	344,473,162	347,056,711	349,659,636	352,282,083	354,924,199	357,586,131	360,268,027	362,970,037
Population growth	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%
Craniopharyngioma prevalence	6,538	6,587	6,637	6,687	6,737	6,787	6,838	6,889	6,941	6,993	7,046	7,098	7,152	7,205	7,259
% PWS prevalence	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%	0.002%
Beloranib treated patients		132	332	669	1,011	1,357	1,368	1,378	1,388	1,399	1,409	1,420	1,430	1,441	1,452
% penetration		2%	5%	10%	15%	20%	20%	20%	20%	20%	20%	20%	20%	20%	20%
Annual cost of therapy	120,000	126,000	132,300	138,915	145,861	153,154	160,811	168,852	177,295	186,159	195,467	205,241	215,503	226,278	237,592
% price increase		5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%	5%
Gross U.S. beloranib sales ($MM)	**0.0**	**16.6**	**43.9**	**92.9**	**147.4**	**207.9**	**219.9**	**232.7**	**246.1**	**260.4**	**275.4**	**291.4**	**308.2**	**326.1**	**345.0**
Gross to net adjustment	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
Net U.S. beloranib sales ($MM)	**0.0**	**14.1**	**37.3**	**79.0**	**125.3**	**176.7**	**186.9**	**197.8**	**209.2**	**221.3**	**234.1**	**247.7**	**262.0**	**277.2**	**293.2**

EU revenue estimates	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
EU population	327,889,391	330,348,561	332,826,175	335,322,372	337,837,289	340,371,069	342,923,852	345,495,781	348,086,999	350,697,652	353,327,884	355,977,843	358,647,677	361,337,535	364,047,566
Population growth	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%	0.75%
Craniopharyngioma prevalence	8,197	8,259	8,321	8,383	8,446	8,509	8,573	8,637	8,702	8,767	8,833	8,899	8,966	9,033	9,101
% PWS prevalence	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%	0.003%
Beloranib treated patients			166	419	845	1,276	1,715	1,727	1,740	1,753	1,767	1,780	1,793	1,807	1,820
% penetration			2%	5%	10%	15%	20%	20%	20%	20%	20%	20%	20%	20%	20%
Annual cost of therapy		80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000	80,000
% price increase		0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Gross U.S. beloranib sales ($MM)	**0.0**	**0.0**	**13.3**	**33.5**	**67.6**	**102.1**	**137.2**	**138.2**	**139.2**	**140.3**	**141.3**	**142.4**	**143.5**	**144.5**	**145.6**
Gross to net adjustment	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%	15%
Net U.S. beloranib sales ($MM)	**0.0**	**0.0**	**11.3**	**28.5**	**57.4**	**86.8**	**116.6**	**117.5**	**118.3**	**119.2**	**120.1**	**121.0**	**121.9**	**122.9**	**123.8**

Source: JMP Securities LLC and Company Reports

MANAGEMENT TEAM

Thomas E. Hughes, Ph.D. – Chief Executive Officer

Thomas E. Hughes, Ph.D. joined Zafgen in 2008 as President, Chief Executive Officer and a member of the company's Board of Directors. Dr. Hughes has over 25 years of experience in pharmaceutical research and development, and from 1987 to 2008, held several positions at Novartis AG (and formerly Sandoz Pharmaceuticals) including Vice President and Global Head of the Cardiovascular and Metabolic Diseases therapeutic area at the Novartis Institutes for BioMedical Research in Cambridge, MA. At Novartis, he oversaw many drug discovery and development projects targeting obesity, diabetes, and heart disease, including efforts to discover and develop its dipeptidyl peptidase IV (DPP-IV) inhibitor vildagliptin (Galvus®/Eucreas®). Dr. Hughes is the author of over 40 peer-reviewed publications and is an inventor on numerous issued and pending patents related to the treatment of diabetes, cardiovascular disease, and obesity. Dr. Hughes also serves as a director on the board of Miragen Therapeutics, Inc., and is a member of several scientific and strategic advisory boards, including Broadview Ventures and Nimbus Discovery, LLC.

Patrick Loustau – President

Mr. Loustau was appointed President of Zafgen in July 2014. He has more than 20 years of experience in U.S. and global management with up to $10.7B P&L in the biopharmaceutical industry. Most recently, Mr. Loustau was the Senior Vice President for Global Commercialization (Cardiovascular & Metabolics) at Bristol-Myers Squibb. Previously, he worked at Novo Nordisk, where he held roles as the Senior Vice President for Global Marketing & Medical Affairs (based in Copenhagen), Vice President, Sales Force and Managed Care/Government Affairs (in Princeton, NJ), President & GM (Toronto), Regional Business Director Sales and Senior Director Marketing Diabetes (both also in Princeton), and Project Leader – Business Acceleration (for Germany, USA & Canada). He began his career with Parke-Davis in Paris, France as an HR and Training Manager. Mr. Loustau is a member of the Board of Directors for the Greater New York Chapter of the American Diabetes Association and has participated in numerous athletic fundraising events for healthcare education and research.

Dr. Dennis D. Kim, M.D., M.B.A. – Chief Medical Officer

Dr. Kim joined Zafgen in September 2011 as the company's Chief Medical Officer. Dr. Kim is a board-certified endocrinologist with more than 10 years of experience in the biotech and medical technology industries. Prior to joining Zafgen, Dr. Kim held multiple senior-level clinical and management positions at Orexigen Therapeutics, EnteroMedics, Inc., and Amylin Pharmaceuticals. Additionally, Dr. Kim is an assistant professor of medicine, division of endocrinology/metabolism, at the University of California, San Diego (UCSD) School of Medicine. He holds an M.D. from the University of Health Sciences, The Chicago Medical School, an M.B.A from UCSD Rady School of Management and a B.S. in biology from the University of California at Los Angeles.

James E. Vath, Ph.D. – Head of Discovery and Development

Dr. Vath joined Zafgen in 2006 and brings over 20 years of experience in the biotechnology and pharmaceutical industries to his role as Head of Discovery and Development. Prior to joining the company, Dr. Vath worked with established companies and new ventures to assess, develop, and execute product development plans. Previously, he served as Senior Vice President of Product Development at Phylogix Inc., and as Senior Vice President of Research at Praecis Pharmaceuticals. Dr. Vath also held roles as Director of Protein Technologies at Millennium Pharmaceuticals and a lab head in development at Genetics Institute. Dr. Vath is a contributing author on numerous peer-reviewed journal publications and book chapters. Dr. Vath earned his Ph.D. in chemistry from the Massachusetts Institute of Technology and a B.S. in chemistry from Northeastern University.

Patricia Allen – Chief Financial Officer

Ms. Allen joined Zafgen as Chief Financial Officer in January 2013. She has 20 years of financial leadership experience in the biotechnology industry at both publicly traded and private companies. For the past two years, she has provided independent consulting services to biotechnology companies in a variety of areas, including interim CFO services, fundraising, deal structures, financial planning, organizational structure, investor relations and business development. Previously, Ms. Allen served as the Vice President of Finance, Treasurer and Principal Financial Officer of Alnylam Pharmaceuticals, between 2004 and 2011. Previously, Ms. Allen served as the Corporate Controller and Director of Finance at Alkermes, Inc. where she worked for 12 years. Ms. Allen graduated Summa Cum Laude from Bryant College with a B.S. in Business Administration.

Alicia Secor – Chief Commercial Officer

Ms. Secor joined Zafgen as Chief Commercial Officer in January 2014. Prior to joining Zafgen, she most recently served as Senior Vice President and Chief Operating Officer of Synageva BioPharma Corp. and previously, Ms. Secor spent fifteen years at Genzyme, a Sanofi Company, where she held various leadership positions, most recently as Vice President and General Manager of Metabolic Diseases. Prior to Genzyme, Ms. Secor held positions at Alkermes in business development, at Centocor (a Johnson & Johnson Company) in clinical and commercial operations, and began her career at Pfizer as a hospital-based sales representative. She received her M.B.A. from Northeastern University, and her B.S. in Healthcare Administration from the University of New Hampshire.

Source: Excerpted from Company Reports

FIGURE 16. Zafgen, Inc. Earnings Model

($ in thousands 000's)	2011	2012	2013	1Q:14	2Q:14E	3Q:14E	4Q:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Revenue														
Beloranib				0	0	0	0	0	0	0	6,669	60,618	145,900	271,491
Other revenue			0	256	0	0	0	256	0	0	0	0	0	0
Total Revenue	**0**	**0**	**0**	**256**	**0**	**0**	**0**	**256**	**0**	**0**	**6,669**	**60,618**	**145,900**	**271,491**
Cost of goods sold	0	0	0	0	0	0	0	0	0	0	1,334	12,124	29,180	54,298
Gross Profit	**0**	**0**	**0**	**256**	**0**	**0**	**0**	**256**	**0**	**0**	**5,335**	**48,494**	**116,720**	**217,193**
Operating expenses														
R&D	11,403	11,544	9,561	3,275	4,913	13,755	15,131	37,073	40,780	44,858	49,344	54,279	59,706	65,677
G&A	1,751	2,247	4,219	1,246	1,371	1,508	1,658	5,783	6,939	10,409	36,431	54,646	62,843	69,128
Total Operating Expenses	**13,154**	**13,791**	**13,780**	**4,521**	**6,283**	**15,263**	**16,789**	**42,856**	**47,720**	**55,267**	**85,775**	**108,925**	**122,550**	**134,805**
Operating income (loss)	**(13,154)**	**(13,791)**	**(13,780)**	**(4,265)**	**(6,283)**	**(15,263)**	**(16,789)**	**(42,600)**	**(47,720)**	**(55,267)**	**(80,440)**	**(60,431)**	**(5,830)**	**82,388**
Interest expense	0	(97)	0	(2)	(2)	(10)	(10)	(24)	(40)	(40)	(40)	(40)	(40)	(40)
Foreign currency gains (losses)	(3)	8	(247)	65	0	0	0	65	0	0	0	0		
Net Income Before Taxes	**(13,157)**	**(13,686)**	**(14,027)**	**(4,198)**	**(6,281)**	**(15,253)**	**(16,779)**	**(42,511)**	**(47,680)**	**(55,227)**	**(80,400)**	**(60,391)**	**(5,790)**	**82,428**
Income tax provision	0	0	0	0	0	0	0	0	0	0	0	0	0	28,850
Net income (loss)	**(13,210)**	**(13,753)**	**(14,240)**	**(4,247)**	**(6,281)**	**(15,253)**	**(16,779)**	**(42,560)**	**(47,680)**	**(55,227)**	**(80,400)**	**(60,391)**	**(5,790)**	**53,578**
EPS														
Basic	**($19.17)**	**($19.38)**	**($19.53)**	**($5.82)**	**($8.37)**	**($0.69)**	**($0.75)**	**($15.64)**	**($2.09)**	**($1.96)**	**($2.79)**	**($2.06)**	**($0.19)**	**$1.75**
Diluted	**($19.17)**	**($19.38)**	**($19.53)**	**($5.82)**	**($8.37)**	**($0.69)**	**($0.75)**	**($15.64)**	**($2.09)**	**($1.96)**	**($2.79)**	**($2.06)**	**($0.19)**	**$1.75**
Weighted shares outstanding														
Basic	689	710	729	729	750	22,207	22,318	11,501	22,764	28,220	28,784	29,360	29,947	30,546
Diluted	689	710	729	729	750	22,207	22,318	11,501	22,764	28,220	28,784	29,360	29,947	30,546
Cash Flow														
Net Income	(13,210)	(13,753)	(14,240)	(4,247)	(6,281)	(15,253)	(16,779)	(42,560)	(47,680)	(55,227)	(80,400)	(60,391)	(5,790)	53,578
Depreciation and amortization	4	11	12	3	3	3	3	12	12	12	12	12	12	12
Stock-based compensation	80	121	395	176	150	150	150	626	626	626	626	626	626	626
Other adjustments	852	226	(1,171)	0	0	0	0	0	0	0	0	0	0	0
Operating burn	**(12,274)**	**(13,395)**	**(15,004)**	**(4,068)**	**(6,128)**	**(15,100)**	**(16,626)**	**(41,922)**	**(47,042)**	**(54,589)**	**(79,762)**	**(59,753)**	**(5,152)**	**54,216**
Cash at start of period	3,717	1,467	9,935	35,517	38,483	135,027	119,927	35,517	103,253	56,212	152,023	72,261	12,508	7,356
Cash from operations	(12,274)	(13,589)	(15,004)	(4,020)	(6,128)	(15,100)	(16,626)	(41,922)	(47,042)	(54,589)	(79,762)	(59,753)	(5,152)	54,216
Cash from investing	(45)	(2)	(17)	(5)	0	0	0	(5)	0	0	0	0	0	0
Cash from financing	10,069	22,059	40,603	6,991	102,672	0	0	109,663		150,400			0	0
Shares issued					6,900					5,000				
Price per share					16			16		32				
Effect of FX				0	0	0	0	0	0	0	0	0	0	0
Cash at end of period	**1,467**	**9,935**	**35,517**	**38,483**	**135,027**	**119,927**	**103,301**	**103,253**	**56,212**	**152,023**	**72,261**	**12,508**	**7,356**	**61,572**

Source: Company reports and JMP Securities LLC

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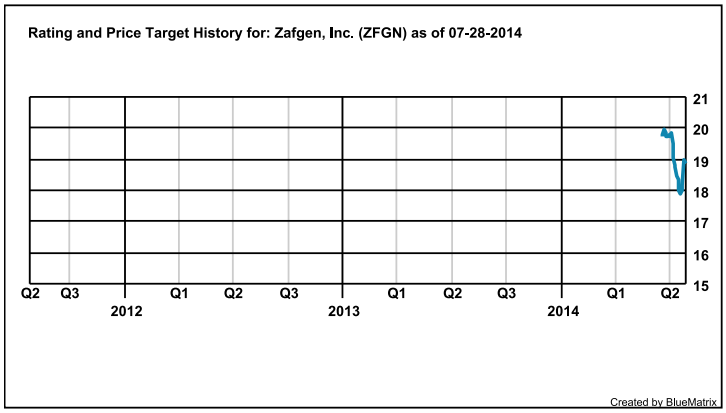
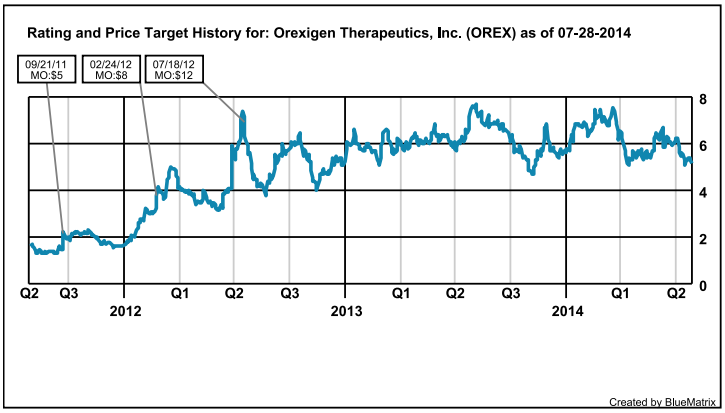
MARKET OUTPERFORM	Buy	266	*59.51%*	Buy	266	*59.51%*	98	*36.84%*
MARKET PERFORM	Hold	141	*31.54%*	Hold	141	*31.54%*	17	*12.06%*
MARKET UNDERPERFORM	Sell	4	*0.89%*	Sell	4	*0.89%*	0	*0%*
COVERAGE IN TRANSITION		36	*8.05%*		36	*8.05%*	0	*0%*
TOTAL:		447	*100%*		447	*100%*	115	*25.73%*

Stock Price Chart of Rating and Target Price Changes:

Note: First annotation denotes initiation of coverage or 3 years, whichever is shorter. If no target price is listed, then the target price is N/A. In accordance with NASD Rule 2711, the chart(s) below reflect(s) price range and any changes to the rating or price target as of the end of the most recent calendar quarter. The action reflected in this note is not annotated in the stock price chart. Source: JMP Securities.





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