Zafgen, Inc. (ZFGN)

Initiating Coverage at Buy and $47 PT

When Obesity Meets Orphan...

Zafgen is anchoring with Orphan indications to build an obesity powerhouse. Zafgen is developing beloranib, an inhibitor of a key metabolic enzyme, methionine aminopeptidase 2 (MetAP2), for the treatment of Prader-Willi syndrome (PWS) and hypothalamic injury associated obesity (HIAO), where obesity is a co-morbidity of these underlying conditions. Both are rare diseases and beloranib has received Orphan Drug Designation for PWS in both the U.S. and EU. Following clinical development in these indications, Zafgen intends to target broader metabolic indications with much larger patient populations such as general obesity and nonalcoholic steatohepatitis (NASH). We believe Zafgen is differentiated from conventional obesity players by focusing on Orphan obesity indications while holding promising potential to address a much larger obesity market with the follow-on programs.

Beloranib slated to address the unmet medical needs in PWS and HIAO. PWS is a genetic disorder. Behavioral and metabolic symptoms associated with PWS are partially due to defects in the hypothalamus. HIAO is caused by physical damage to the hypothalamus, primarily due to surgical removal of a brain tumor. Among all the clinical manifestations of the diseases, our expert consultants noted that hyperphagia (constant sense of hunger) and obesity are the most concerning issues with no drugs approved by the FDA to date.
Zafgen has completed six randomized placebo-controlled clinical trials in over 250 patients for beloranib for three indications: PWS, HIAO, and severe/complicated obesity. Results to date have demonstrated clinically meaningful efficacy and a benign safety profile. Despite changes in clinical trial design, we believe there is a high probability of success for the ongoing ZAF-311 Phase III trial for beloranib in PWS. Top-line data for the six-month randomized period is expected by 1Q16 and is the most imminent/impactful catalyst for Zafgen shares.

A strong balance sheet likely supports a position of strength for Zafgen. With net proceeds of ~$130M from a financing in January 2015 and a total cash position of ~$234M at the end of 1Q15, we believe Zafgen has enough cash to sustain operations into YE16.

Our differentiated viewpoint: we conducted a detailed comparison of beloranib between the ongoing Phase III trial for PWS and previously competed ones, and believe a high likelihood of success for the Phase III trial. We conducted a deep dive into the obesity space and identified key issues for the lackluster commercial adoption. We believe beloranib is differentiated and these issues are largely non-existent for beloranib.

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SEE PAGE 73 FOR REQUIRED DISCLOSURE INFORMATION

Initiate Buy

Price Target: $47.00

Price (Jun. 15, 2015)	$35.60
52-Wk Range	$51.34-$16.51
Market Cap ($M)	$958
ADTV	211,415
Shares Out (M)	26.9
Short Interest Ratio/% Of Float	8.3%
TR to Target	32.0%

Cash Per Share	$8.70
Long-Term Debt/Total Cap	0%
Cash And Equivalents ($M)	$234.2
Enterprise Value ($M)	$723.2

	2014A	2015E		2016E	
		Curr.	Prior	Curr.	Prior
EPS					
1Q	(6.11)	(0.50)A	--	--	NA
2Q	(2.96)	(0.73)	--	--	NA
3Q	(0.65)	(0.74)	--	--	NA
4Q	(0.47)	(0.75)	--	--	NA
FY	(3.00)	(2.72)	--	(2.96)	--
P/E	NM	NM		NM	
Consensus EPS					
FY	--	(2.96)	--	(2.98)	--
FYE Dec					

Zafgen Bull / Bear / STRH Scenarios

Bull Case	Bear Case	STRH case
● Price target $82; 130% upside; 15% probability	● Price target $25; 30% downside; 15% probability	● Price target $47; 31% upwnside; 70% probability
We apply the same following valuation parameters to all cases		
● Discounted earnings model: 25x FY2020 EPS; 25% discount rate ● Discounted cashflow model: 12% discount rate; 0% perpetual growth rate ● Clinical net present value model: economics 100%; profitability 85% ● We do not include the valuation for beloranib in treating severe obesity patients or any of Zafgen's follow-on programs in all of the scenarios of our model		
● Beloranib is widely adopted by physicians and patients alike; it achieves a peak market penetration of 45% for both indications (PWS and HIAO) in both the U.S. and EU ● Assumes a higher prevalence rate for PWS in the U.S. (1:15,000 vs. 1:18,000 in the STRH case) ● Assumes a probability of success of 75% for Zafgen in the discounted cash flow model; assumes a probability of success of 70% and 80% for the PWS and HIAO programs, respectively, in the clinical NPV model	● Assumes beloranib achieves a lower peak market penetration of 35% for both indications (PWS and HIAO) in the U.S. ● Assumes a lower prevalence rate for PWS in the U.S. (1:20,000 vs. 1:18,000 in the STRH case) ● Assumes beloranib faces elevated pricing pressure and receives a net WAC of ~$105K per patient per year for both indications in the U.S. and ~$84K in the EU in 2020	● In the U.S., beloranib achieves a peak market penetration of 40% for both indications; in the EU, beloranib achieves a peak market penetration of 30% for PWS and 35% for HIAO ● Assumes PWS prevalence is 1:18,000 in the U.S. ● Assumes a probability of success of 65% for Zafgen in the discounted cash flow model; assume a probability of success of 60% and 70% for the PWS and HIAO programs, respectively, in the clinical NPV model ● Assumes beloranib receives a net WAC of ~$131K per patient per year for both indications in the U.S. and ~$105K in the EU in 2020

Source: SunTrust Robinson Humphrey

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ZAFGEN, INC.

Zafgen is a clinical stage biopharmaceutical company developing treatments for rare obesity diseases including Prader-Willi syndrome (PWS) and hypothalamic injury associated obesity (HIAO), as well as severe and complicated obesity. Zafgen has completed six placebo controlled human clinical trials with promising data and is conducting two clinical trials for its lead product candidate beloranib, an inhibitor of MetAP2, an enzyme that modulates the activity of key cellular processes that control metabolism. Zafgen is conducting a Phase III trial for beloranib in PWS with top-line data expected in 1Q16 and a Phase IIb trial for beloranib in severe and complicated obesity with interim data expected in 4Q15/1Q16. Zafgen was founded in November 2005 and is headquartered in Boston, MA. The Company completed an IPO in June 2014.

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Senior Management	
Thomas E. Hughes, Ph.D.	CEO
Patrick Loustau	President
Patricia Allen, CPA	CFO
Dennis D. Kim, MD, MBA	CMO
Alicia Secor	Chief Commercial Officer
James E. Vath, Ph.D.	Head of Discovery & Development

Capitalization	
Long-Term Debt (MM):	$0
Market Value of Equity (MM):	$957
Cash (MM):	$234
Technology Value (MM):	$723

Drug Candidate	Stage	Indication
Beloranib	Phase III	Prader-Willi Syndrome (PWS)
	Post-Phase IIa	Hypothalamic injury associated obesity (HIAO)
	Phase IIb	Severe obesity
ZGN-839	Preclinical	NASH / Type II diabetes
2nd-Gen MetAP2i	Preclinical	General obesity

Source: Zafgen public filings and SunTrust Robinson Humphrey

Investment Thesis

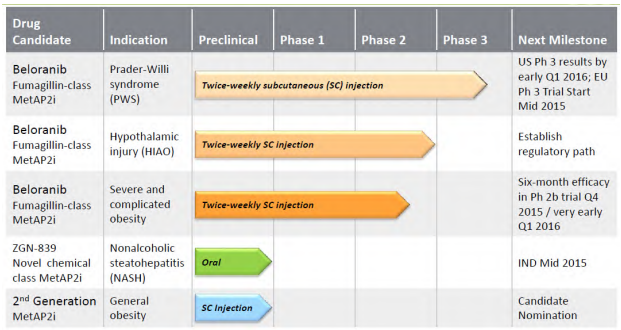
Zafgen is Anchoring with Orphan Indications to Build an Obesity Powerhouse

Zafgen is developing therapeutics for Orphan indications where obesity is a co-morbidity of an underlying condition. The Company is also pursuing the development of therapeutics for more prevalent metabolic diseases. Zafgen's lead product candidate, beloranib, is an inhibitor of methionine aminopeptidase 2 (MetAP2), an enzyme that modulates metabolism. Beloranib is being developed to treat Prader-Willi syndrome (PWS), hypothalamic injury associated obesity (HIAO), as well as severe and complicated obesity. Beloranib received Orphan Drug Designation for the treatment of PWS in both the U.S. and EU.

Following clinical development and a potentially swift regulatory approval for beloranib in PWS and HIAO as well as the potential to charge a premium price, Zafgen intends to develop a second generation MetAP2i therapeutic to treat broader metabolic indications such as general obesity and nonalcoholic steatohepatitis (NASH), a disease of the liver associated with obesity. Both general obesity and NASH are much larger indications with regard to patient number and market size as compared to PWS and HIAO.

We believe Zafgen's strategy is differentiated from other conventional obesity players such as Vivus, Arena and Orexigen by focusing on Orphan obesity indications. Zafgen at the same time also holds promising potential to address a much larger obesity market with the Company's follow-on programs.

Exhibit 1: Zafgen's Clinical and Preclinical Pipeline



Source: Zafgen public presentation

Rich Catalysts Are Expected in the Next 12 Months

Zafgen is advancing multiple clinical programs with several major catalysts expected in the next six to 12 months. Zafgen is conducting a pivotal Phase III clinical trial ZAF-311 (Beloranib Efficacy Safety and Tolerability in PWS, or bestPWS) for beloranib in treating PWS. Zafgen believes the pivotal Phase III clinical program will consist of two Phase III trials, one in the U.S. (ZAF-311 or bestPWS), and the other in the EU (ZAF-312 or bestPWS│EU). The randomized trial will evaluate the efficacy and safety of beloranib in 108 PWS patients over a six-month period of treatment followed by a six-month open-label extension. Zafgen expects to report top-line data for the six-month randomized period by 1Q16, which we believe is the most imminent and impactful catalyst for Zafgen shares.

After completing the ZAF-221 Phase IIa proof-of-concept clinical trial for beloranib in treating HIAO, Zafgen is establishing a regulatory pathway for this program in the U.S. and EU with updates planned in 2015 and the initiation of the Phase III program in 2016, which are meaningful catalysts. Due to a superior efficacy and benign safety profile demonstrated in the ZAF-221 Phase IIa trial, we believe there is a high probability of success for the Phase III program if there is no major deviation in trial design. Our pediatric endocrinology consultant who is familiar with the trial noted that the Phase IIa trial demonstrated very clean data and had no reason to believe that the Phase III program would fail other than the small patient number having been studied to date.

Zafgen expects to report six-month interim data for the ZAF-203 Phase IIb trial for beloranib in treating severe obesity patients with type 2 diabetes in 4Q15/1Q16. We have not included this program in our valuation models due to the early nature of the program and uncertainties associated with the regulatory pathway going forward. However, we believe success of this trial could be important in establishing the effects of beloranib beyond Orphan indications to a broader obesity population and could provide additional upside potential for investors.

Exhibit 2: Catalysts for Zafgen Expected in 2015 and 2016

Program	2015	2016
Beloranib PWS	• Complete enrollment in US Phase III trial • Initiate EU Phase III trial mid 2015	➡ • Six month results from US 'bestPWS' trial in early 1Q • Initiate pediatric program • Injector device development
Beloranib HIAO	➡ • Establish US/EU regulatory path • Obtain orphan designation in US and EU	➡ • Initiate Phase III program
Beloranib Severe Obesity	➡ • Six month Phase IIb data readout 4Q15/1Q16	• Complete Phase IIb • Development decision point
ZGN-839 NASH	• Complete preclinical profiling • File IND mid-2015	• Complete Phase I PK/ Safety/Tolerability trials
Second-Generation MetAP2i Obesity	• Complete preclinical profiling • Development candidate nomination	• IND 1Q • Initiate Phase I trial

Note: arrows indicate more impactful catalysts; Source: Zafgen public presentation, SunTrust Robinson Humphrey

Beloranib Addresses Unmet Medical Needs for both PWS and HIAO

PWS is a rare genetic disorder caused by abnormalities on the chromosome 15. Behavioral and metabolic symptoms associated with PWS are partially due to defects in the hypothalamus. PWS affects approximately 1 in 20,000 people in the U.S. and 1 in 25,000 in the EU, which translates to approximately 16,000 and 20,000 PWS patients in the U.S. and EU, respectively. Among all the clinical manifestations of the disease, our expert consultants noted that hyperphagia, which is a constant sense of hunger, and obesity resulting from hyperphagia and overeating are the most concerning issues for PWS patients. Obesity associated metabolic complications, including cardiovascular disease, diabetes, and sleep apnea, are the primary causes of mortality for PWS patients. Hyperphagia behaviors, including sneaking and stealing food, seeking food in trash, seeking food in the late night, and eating items not fit for human consumption (e.g., animal food, spoiled food, decorative items that look like food, garbage, etc.), impair the PWS patients' ability to engage in normal social activities, such as living independently or attending school/work. To date there has been no FDA approved therapeutics for the management of obesity or hyperphagia for PWS patients. Our pediatric endocrinology consultant assigned an unmet need value of 10 for hyperphagia and a value of eight for obesity on a scale of one to ten, with one being no unmet need and 10 being the most significant unmet need.

HIAO patients demonstrate varying levels of hyperphagia and obesity due to impairment of the hypothalamus, similar to PWS. However, HIAO differs in that the hypothalamus impairment is most frequently caused by the surgical removal of craniopharyngioma, a type of benign brain tumor. The prevalence of a craniopharyngioma is approximately 1:50,000 in the U.S. and EU, and it is estimated that between 30% and 77% of patients will develop HIAO after removing surgically removing the craniopharyngioma.

Zafgen's beloranib is a first-in-class small molecule that inhibits methionine aminopeptidase 2, which is an important enzyme in controlling metabolism. The exact mechanism of action for beloranib is not fully elucidated. But *in vitro* data suggest that beloranib addresses appetite control and energy consumption peripherally by increasing fatty acid oxidation and suppressing lipid and cholesterol biosynthesis, which is different from what has been employed by previously approved anti-obesity agents.

The ZAF-211 and ZAF-221 Phase IIa proof-of-concept trials for PWS and HIAO, respectively were successful in demonstrating clinically meaningful efficacy (reduction in body weight, body fat, and hyperphagia behavior in ZAF-211, and reduction in body weight in ZAF-221) and good tolerability.

We believe beloranib has the potential to address significant unmet needs in both the PWS and HIAO indications.

In our revenue build-up model, we project Zafgen to book ~$1B in revenue for beloranib for the treatment of PWS ($650M in the U.S. and $350M in the EU), and $260M for beloranib for the treatment of HIAO ($140M in the U.S. and $120M in the EU), in the out-year of our model, 2025.

In our projections, we do not include the market potential of the larger general obesity market of varying severities or the NASH population, which represent additional upside potential and long-term growth for investors.

Exhibit 3: Zafgen Revenue Build-Up Model

	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Beloranib for Prader-Willi Syndrome (PWS)											
U.S.											
U.S. population	318.9	321.2	323.4	325.7	328.1	330.4	332.7	335.1	337.5	339.9	342.3
Prevalence rate of PWS	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*	*1/18,000*
Number of PWS patients, U.S.	17,717	17,842	17,969	18,097	18,225	18,355	18,485	18,616	18,748	18,881	19,016
% of PWS patients > 12 years of age	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
# of PWS patients > 12 years of age	8,858	8,921	8,985	9,048	9,113	9,177	9,242	9,308	9,374	9,441	9,508
Diagnoses rate of PWS	*75.0%*	*75.0%*	*75.0%*	*76.0%*	*77.0%*	*78.0%*	*79.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*
Diagnosed PWS patients, U.S.	13,288	13,382	13,477	13,754	14,033	14,317	14,603	14,893	14,999	15,105	15,212
% of diagnosed PWS patients who are obese	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*
# of diagnosed PWS patients who are obese, U.S.	10,630	10,705	10,781	11,003	11,227	11,453	11,682	11,914	11,999	12,084	12,170
Treatment rate of obese PWS patients				*60.0%*	*65.0%*	*70.0%*	*75.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*
Drug-treat obese PWS patients, U.S.				6,602	7,297	8,017	8,762	9,531	9,599	9,667	9,736
% Market penetration by beloranib				*5.0%*	*20.0%*	*30.0%*	*35.0%*	*37.0%*	*38.5%*	*40.0%*	*40.0%*
# of PWS patients receiving beloranib treatment, U.S.				330	1,459	2,405	3,067	3,527	3,696	3,867	3,894
WAC				$31,250	$125,000	$131,250	$137,813	$144,703	$151,938	$159,535	$167,512
Total U.S. sales revenue for PWS booked by Zafgen ($MM)				**10.3**	**182.4**	**315.7**	**422.6**	**510.3**	**561.5**	**616.9**	**652.4**
EU											
EU population	505.7	506.7	507.7	508.7	509.8	510.8	511.8	512.8	513.8	514.9	515.9
Prevalence rate of PWS	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*	*1/25,000*
Number of PWS patients, EU	20,228	20,268	20,309	20,350	20,390	20,431	20,472	20,513	20,554	20,595	20,636
% of PWS patients > 12 years of age	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
# of PWS patients > 12 years of age	10,114	10,134	10,154	10,175	10,195	10,216	10,236	10,256	10,277	10,298	10,318
Diagnoses rate of PWS	*70.0%*	*70.0%*	*70.0%*	*71.0%*	*72.0%*	*73.0%*	*74.0%*	*75.0%*	*75.0%*	*75.0%*	*75.0%*
Diagnosed PWS patients, EU	14,160	14,188	14,216	14,448	14,681	14,915	15,149	15,385	15,415	15,446	15,477
% of diagnosed PWS patients who are obese	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*
# of diagnosed PWS patients who are obese, EU	11,328	11,350	11,373	11,559	11,745	11,932	12,119	12,308	12,332	12,357	12,382
Treatment rate of obese PWS patients				*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*
Durg-treat obese PWS patients, EU				8,091	8,221	8,352	8,484	8,615	8,633	8,650	8,667
% Market penetration by beloranib				*3.0%*	*15.0%*	*20.0%*	*22.5%*	*25.0%*	*27.5%*	*30.0%*	*30.0%*
#of PWS patients receiving beloranib treatment, EU				243	1,233	1,670	1,909	2,154	2,374	2,595	2,600
WAC				$25,000	$100,000	$105,000	$110,250	$115,763	$121,551	$127,628	$134,010
Total EU sales revenue for PWS booked by Zafgen ($MM)				**6.1**	**123.3**	**175.4**	**210.4**	**249.3**	**288.6**	**331.2**	**348.4**
Total WW revenue booked by Zafgen for beloranib in PWS ($MM)				**16.4**	**305.8**	**491.1**	**633.1**	**759.7**	**850.1**	**948.1**	**1,000.8**
Beloranib for Hypothalamic Injury Associated Obesity (HIAO)											
U.S.											
U.S. adolescent and adult population	271.1	273.0	274.9	276.9	278.8	280.8	282.8	284.8	286.8	288.9	290.9
Prevalence rate of craniopharyngioma	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*
Number of craniopharyngioma patients, U.S.	5,421	5,460	5,499	5,538	5,577	5,617	5,656	5,697	5,737	5,778	5,819
% of craniopharyngioma patients undergoing surgery	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*
# of craniopharyngioma patients undergoing surgery, U.S.	4,337	4,368	4,399	4,430	4,462	4,493	4,525	4,557	4,590	4,622	4,655
% of craniopharyngioma patients develop HIAO after surgery	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
# of craniopharyngioma patients develop HIAO after surgery, U.S.	2,169	2,184	2,199	2,215	2,231	2,247	2,263	2,279	2,295	2,311	2,327
Treatment rate of obese craniopharyngioma patients	*90.0%*	*90.0%*	*90.0%*	*90.0%*	*90.0%*	*90.0%*	*90.0%*	*90.0%*	*90.0%*	*90.0%*	*90.0%*
Durg-treat obese craniopharyngioma patients, U.S.	1,952	1,966	1,979	1,994	2,008	2,022	2,036	2,051	2,065	2,080	2,095
% Market penetration by beloranib						*15.0%*	*20.0%*	*30.0%*	*35.0%*	*37.5%*	*40.0%*
# of PWS patients receiving beloranib treatment, U.S.						303	407	615	723	780	838
WAC						$131,250	$137,813	$144,703	$151,938	$159,535	$167,512
Total U.S. sales revenue for HIAO booked by Zafgen ($MM)						**39.8**	**56.1**	**89.0**	**109.8**	**124.4**	**140.4**
EU											
EU adolescent and adult population	442.5	443.4	444.3	445.1	446.0	446.9	447.8	448.7	449.6	450.5	451.4
Prevalence rate of craniopharyngioma	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*	*1/50,000*
Number of craniopharyngioma patients, EU	8,850	8,867	8,885	8,903	8,921	8,939	8,956	8,974	8,992	9,010	9,028
% of craniopharyngioma patients undergoing surgery	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*	*70.0%*
# of craniopharyngioma patients undergoing surgery, EU	6,195	6,207	6,220	6,232	6,245	6,257	6,270	6,282	6,295	6,307	6,320
% of craniopharyngioma patients develop HIAO after surgery	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*	*50.0%*
# of craniopharyngioma patients develop HIAO after surgery, EU	3,097	3,104	3,110	3,116	3,122	3,129	3,135	3,141	3,147	3,154	3,160
Treatment rate of obese craniopharyngioma patients	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*	*80.0%*
Durg-treat obese craniopharyngioma patients, EU	2,478	2,483	2,488	2,493	2,498	2,503	2,508	2,513	2,518	2,523	2,528
% Market penetration by beloranib						*12.5%*	*15.0%*	*25.0%*	*30.0%*	*32.5%*	*35.0%*
# of PWS patients receiving beloranib treatment, EU						313	376	628	755	820	885
WAC						$105,000	$110,250	$115,763	$121,551	$127,628	$134,010
Total EU sales revenue for HIAO booked by Zafgen ($MM)						**32.8**	**41.5**	**72.7**	**91.8**	**104.6**	**118.6**
Total WW revenue booked by Zafgen for beloranib in HIAO ($MM)						**72.7**	**97.6**	**161.7**	**201.6**	**229.1**	**258.9**
Total WW revenue booked by Zafgen for beloranib in PWS and HIAO ($MM)				**16.4**	**305.8**	**563.7**	**730.7**	**921.4**	**1,051.7**	**1,177.2**	**1,259.7**

Source: SunTrust Robinson Humphrey

The following assumptions are applied with regard to the clinical development timeline for beloranib in the PWS and HIAO programs.

Beloranib for the treatment of PWS

- ZAF-311 Phase III trial: six-month data in 1Q16, 12-month data in 3Q16
- ZAF-312 Phase III trial: initiate in mid-15, complete enrollment in mid-16, 12-month data in mid-17
- Pre-NDA meeting and NDA submission: YE17
- FDA approval: mid-18 under six-month priority review
- Launch: beloranib in 2H18 for the treatment of PWS

Beloranib for the treatment of HIAO (assume similar timeframe with the PWS program with a 1.5 years lag)

- First Phase III trial: initiate in 1Q16, six-month data in 3Q17
- Second Phase III trial: initiate by YE16, complete enrollment by YE17, 12-month data by YE18
- Pre-NDA meeting and sNDA submission: mid-19
- FDA approval: YE19 under six-month priority review
- Launch: beloranib in 4Q19 or 1Q20 for the treatment of HIAO

Zafgen Has Completed Six Clinical Trials for Beloranib Demonstrating Consistent and Promising Results

Zafgen has completed six randomized placebo-controlled clinical trials in over 250 patients for three different indications related to obesity: PWS, HIAO, and severe/complicated obesity. We believe such a wealth of clinical data are valuable in understanding the drug and in potentially predicting the outcome of the ongoing ZAF-311 Phase III trial in PWS and ZAF-203 Phase IIb trial in treating severe obesity.

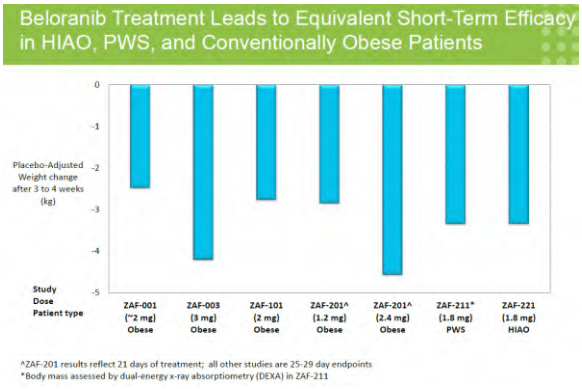
Exhibit 4: Zafgen Ongoing and Completed Clinical Trials for Beloranib

Trial Name	Phase	Indication	Trial Type	Dosing Regimen	Treatment	Pts Number	BMI (kg/m^2)
Completed Trials							
ZAF-001	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• Escalating doses of 0.1mg/m^2, 0.3mg/m^2, and 0.9mg/m^2, or ~0.2mg, 0.6mg, and 2mg • IV BIW	4 weeks	31 (all female)	32-45
ZAF-003	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• 3.0mg, 6.0mg, and 2.5mg • 3.0mg and 6.0mg given IV BIW for 4 weeks • 2.5mg given IV BIW for the 1st week and QW for the subsequent 6 weeks	4 weeks or 7 weeks	25 (all female)	30-50
ZAF-101	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• 1.0mg, 2.0mg, and 4.0mg • SubQ BIW	4 weeks	25 (all female)	30-45
ZAF-201	IIa	Severe Obesity	Randomized, DB, Placebo-controlled	• 0.3mg, 0.6mg, 1.2mg, 2.4mg, and 3.2mg • SubQ BIW	12 weeks	160 (157 female)	30-50
ZAF-211	IIa	PWS	Randomized, DB, Placebo-controlled	• 1.2mg and 1.8mg • SubQ BIW	4 weeks	17	26-44
ZAF-221	II	HIAO	Randomized, DB, Placebo-controlled	• 1.8mg • SubQ BIW	4 weeks + 4 weeks extension	14	30-55
Ongoing Trials							
ZAF-203	IIb	Severe Obesity with T2D	Randomized, DB, Placebo-controlled	1.2mg and 1.8mg SubQ BIW	12 months with 6 months interim	150	30-60
ZAF-311 (bestPWS)	III	PWS	Randomized, DB, Placebo-controlled	1.8mg, 2.4mg SubQ BIW	6 months + 6 months open label	108	Age 12-17: BMI≥ 95th percentile for age and gender, Age 18+: BMI 27-60

Note: DB, double blind; Source: Zafgen public filings, SunTrust Robinson Humphrey

Beloranib has demonstrated rapid and consistent short-term efficacy across all three indications. We believe the consistent weight reduction observed is very meaningful and encouraging.

Exhibit 5: Placebo-Adjusted Weight Change for Beloranib across Completed Trials



*Note: ^ZAF-201 results reflect 21 days of treatment; all other studies are 25-29 day endpoints; *body mass assessed by dual-energy x-ray absorptiometry (DEXA) in ZAF-211; Source: Zafgen public presentation*

Beloranib has been generally well-tolerated with no safety concerns, specifically among PWS and HIAO patients. Sleep disturbances and other sleep related tolerability issues have resulted in a high withdrawal rate in the 2.4mg beloranib arm in the ZAF-201 Phase IIa trial in severe obesity patients. Zafgen is applying various strategies to mitigate this issue in the ongoing ZAF-203 Phase IIb trial, which includes the employment of a lower dose of 1.8mg to replace the 2.4mg dose used in the ZAF-201 trial, and up-titration for patients in the 1.8mg arm with 1.2mg beloranib for four weeks. Importantly, our expert consultants note that sleep disturbances and sleep latency should not be an issue for PWS or HIAO patients due to hyper-somnolence being commonly observed among these patients at baseline.

We Expect a High Probability of Success from the Phase III Trials for Beloranib in PWS

We believe that there is a high likelihood of success for the ongoing Phase III ZAF-311 (bestPWS) trial for beloranib in the treatment PWS. We believe previously completed clinical trials, specifically the ZAF-211 Phase IIa trial for the treatment of PWS, the ZAF-201 Phase IIa trial for severe obesity, and the ZAF-221 Phase IIa trial for HIAO, were largely successful in reducing body weight, body mass, and fat mass, in improving cardio-metabolic biomarkers, and in improving hyperphagia behaviors. Compared to the ZAF-211 Phase IIa trial for the treatment of PWS, several changes have been made to the ongoing ZAF-311 Phase III trial after discussions with the FDA, including a higher dose (1.8mg/2.4mg vs. 1.2mg/1.8mg), a longer treatment duration (six months vs. four weeks), less time spent in PWS group homes (<50% vs. 100%), and the employment of co-primary endpoints, weight loss and change in hyperphagia-related behavior. Please refer to Exhibit 34 at page 36 for an in-depth comparison/contrast of the ZAF-311 trial and the ZAF-211 and ZAF-201 clinical trials.

We have conducted a detailed analysis and believe that the changes are a net-positive for Zafgen and we conservatively assign a 60% probability of success for the ongoing ZAF-311 Phase III trial in our financial models. This is based on our conviction that:

- The 2.4mg dose of beloranib should be reasonably tolerated in PWS patients due to hypersomnolence being commonly observed among PWS patients at baseline.
- A placebo-adjusted weight reduction from 7.9mg to 15.7mg could be attainable in the 1.2mg or 2.4mg beloranib arms employed in the ZAF-311 Phase III trial at the end of the six-month treatment period after comparing the long-term durability of commercialized obesity drugs on the U.S. market.
- Limiting the time spent in PWS group homes (<50% vs. 100%) for PWS patients could minimize variation in reporting hyperphagia related behaviors and increase patient compliance with the clinical trial protocol. The previous lack of compliance was the main reason for the large variation in weight reduction data observed in the ZAF-211 Phase IIa trial, according to Zafgen.
- The co-primary endpoints are a more stringent requirement as compared to a single primary endpoint (one of the two components of the co-primary endpoints). We believe the co-primary endpoints could be achieved based on promising data from previous trials and the power assumptions of the ZAF-311 trial (90% powered to demonstrate a 1.5% reduction of body weight and 4.5 units reduction in the PWS questionnaire). Even if only one of the clinical endpoints is met with statistical significance, our expert consultants suggest that the drug could still have a clinically meaningful benefit for PWS patients. Under this scenario, management commented that they would still move forward with a regulatory submission. We believe FDA could look at the totality of the data to determine the approvability of the drug.

Differentiated from Conventional Obesity Drugs, Physician Utilization and Payer Coverage for Beloranib Should not be a Problem

The obesity space has been at the top of investor's radar screens since the late 2000s and early 2010s due to the large size of the addressable market and a historical lack of effective treatments. However, the recently approved obesity drugs, including Vivus's Qsymia, Arena's Belviq, Orexigen's Contrave, and Novo Nordisk's Saxenda, have not been widely adopted by physicians, and stock prices for VVUS, ARNA, and OREX have been lackluster since the launch of these drugs.

We believe beloranib is differentiated from these conventional obesity drugs and that physician utilization and payer coverage could be more favorable for beloranib, primarily due to:

- Target indication and physician perception of the diseases
- The prescriber base
- The novelty of the compounds

Exhibit 6: Comparison between Beloranib and Conventional Obesity Players

	CATEGORY	BELORANIB	TRADITIONAL OBESITY PLAYERS	IMPLICATION TO ZAFGEN
Different	Indication	Orphan disease: PWS, HIAO, etc.	Primary care disease: obesity	Ability to charge premium pricing Payer coverage likely more readily
Different	Treating physician	Pediatrician	Mostly PCP and endocrinologist	Perception of disease and sensitivity to drug pricing different
Different	Physician perception of disease	PWS, HIAO are viewed as diseases	Obesity is not unanimously viewed as disease by physicians	Prescribers are much more willing to prescribe beloranib to treat "real" diseases
Different	Composition of drug	New chemical entity	Qsymia and Contrave are repurposed generic combos	Off-label use largely absent
Different	Route of administration	SubQ twice per week	Oral BID or QD	SubQ is less desirable than oral, but on par with most orphan drugs
Same	Review division within FDA	All drugs reviewed by Division of Metabolism and Endocrinology Products (DMEP) in FDA		Relatively more predictable regarding clinical trial requirement

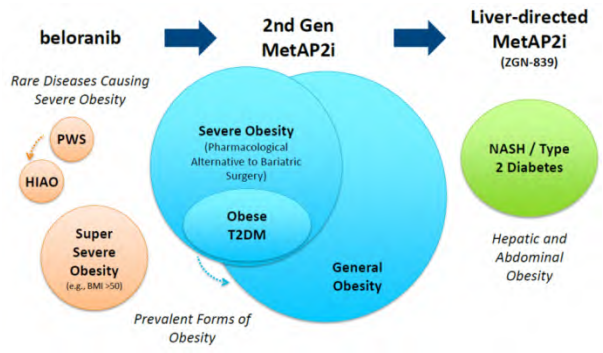
Source: SunTrust Robinson Humphrey

Zafgen Intends to Target the Larger General Obesity and NASH Markets in Follow-on Programs

Zafgen plans to develop other MetAP2 inhibitors to address the indications of general obesity and NASH. General obesity and NASH are much larger markets as compared to PWS and HIAO in terms of patient number: obesity affects approximately one third, and NASH affects one tenth of the U.S. population, or approximately 100,000,000 and 30,000,000, respectively. However, clinical development requires much larger trial sizes (over 4,500 for obesity and approximately 2,500 for NASH) and longer duration of treatment (over one year). Physician adoption and payer reimbursement will be more difficult than for Orphan indications.

We have not included either indication in our financial models and believe they could provide additional upside potential for Zafgen shares with the advent of additional positive clinical data.

Exhibit 7: Zafgen Corporate Strategy



Note: size of bubble represents relative size of patient population; Source: SunTrust Robinson Humphrey adapted from Zafgen public presentation

Recent Financing Strengthens Balance Sheet

In January 2015 Zafgen announced the closing of a public offering of common shares with net proceeds of approximately $129.6 million. The Company ended 1Q15 with a total cash position of

approximately $234 million. With a much strengthened balance sheet, Zafgen plans to develop beloranib for multiple indications along with progressing the ZAF-839 program for NASH. Total operating expenses for 1Q15 were approximately $13.2 million due to increased costs associated with the beloranib program, ZGN-839 and other early stage development programs. We project R&D costs to increase in the coming quarters based on the ongoing ZAF-311 Phase III trial and other planned clinical trials including the ZAF-312 Phase III clinical trial in the EU. We model current cash and cash equivalents as sufficient to sustain Zafgen's operations into YE16.

Valuation Summary

We value ZFGN shares by employing four distinct methodologies. In our discounted earnings model we discount estimated earnings per share from the first year of meaningful revenue back to 12 months from the current period while applying a reasonable, market centric, multiple and discount rate which takes into account the relevant competitive landscape and probability of success. We assume profitability for Zafgen in 2019 and in the following year, 2020, Zafgen to have meaningful positive EPS of $4.91. We apply a 25x multiple that is in-line with the mean estimated 2015 EPS of an aggregate of select profitable biotechnology companies. We then discount back by 25%, which takes into consideration the clinical, regulatory, and commercial risks associated with the development and commercial success potential of Zafgen's assets. The application of these metrics results in a target price of $44.94.

Exhibit 8: Zafgen Discounted Earnings Model

Diluted	$4.91
PE	25
Discount Years	4.5
Discount Rate	25.0%
Valuation	$44.94

Forward P/E Ratio	Discount Rate 55.0%	50.0%	45.0%	40.0%	35.0%	30.0%	25.0%	20.0%
15x	$10.24	$11.87	$13.83	$16.19	$19.07	$22.60	$26.97	$32.40
20x	13.66	15.83	18.44	21.59	25.43	30.14	35.95	43.20
25x	17.07	19.78	23.05	26.99	31.79	37.67	44.94	54.00
30x	20.48	23.74	27.65	32.39	38.14	45.20	53.93	64.81
35x	23.90	27.70	32.26	37.78	44.50	52.74	62.92	75.61
40x	27.31	31.66	36.87	43.18	50.86	60.27	71.91	86.41
45x	30.73	35.61	41.48	48.58	57.22	67.81	80.90	97.21
50x	34.14	39.57	46.09	53.98	63.57	75.34	89.88	108.01
55x	37.56	43.53	50.70	59.37	69.93	82.87	98.87	118.81

Sources: SunTrust Robinson Humphrey

We additionally construct a risk-adjusted discounted cash flow (DCF) model and discount the projected future cash flows of Zafgen back to reach a 12-month target price of $47.57. From our revenue build-up model, we estimate cash flow of $452 million from the Company in 2025. We employ a biotech universe-standard discount rate of 12% and a perpetual growth rate of 0% to be conservative.

Exhibit 9: Zafgen DCF Model

Final year FCF	452
Perpetual Growth Rate	0.0%
Terminal Value	**3,769**
Discount Factor	0.30
Present Value of Terminal Value	**1,141**
Present Value of Cash Flows	**593**
Enterprise Value	**1,734**
Add: Net cash	234
Market Value	**1,968**
Fully Diluted Shares Outstanding	26.9
Value per Fully Diluted Share	**$73.18**
Prabability of success	65%
Risk adjusted value per fully diluted share	**$47.57**

Sources: SunTrust Robinson Humphrey

A third methodology we rely upon is the clinical net present value (NPV) model which is based on our peak revenue estimate for beloranib for both PWS and HIAO. We estimate peak revenue for beloranib in the PWS indication of approximately $617 million in the U.S. and $331 million in the EU; and peak revenue for beloranib in the HIAO indication of approximately $124 million in the U.S. and $105 million in the EU. We assign a probability of success of 60% for the PWS program and 70% for the HIAO program based on the clinical profiles demonstrated to date. We also assign 100% of the U.S. revenue to Zafgen and a back-end royalty of 15% of the EU economics to Zafgen. Taking into account the number of current shares outstanding, we obtain a clinical NPV of $47.65 per share for beloranib in both the PWS and HIAO indications.

Exhibit 10: Zafgen Clinical NPV Model

Drug name	Indication	Status	Launch	Success	Peak Sales (US$m)	Economics	Profitability	NPV (US$)
Beloranib	PWS (U.S.)	Phase III	2018	60%	617	100%	85%	24.19
Beloranib	PWS (EU)	Phase III	2018	60%	331	100%	85%	12.99
Beloranib	HIAO (U.S.)	Phase IIa completed	2020	70%	124	100%	85%	5.69
Beloranib	HIAO (EU)	Phase IIa completed	2020	70%	105	100%	85%	4.79
							Total	**47.65**

Sources: SunTrust Robinson Humphrey

Finally we utilize a comparable-company analysis, which is comprised of biotech companies with compounds targeting Orphan indications in both the endocrine and metabolic field. We then compare the median enterprise value (EV) of the comparable universe ($1,177 million) to the EV of Zafgen ($723 million). The comparison demonstrates that Zafgen shares are currently trading at a discount of 39% to the median EV of the comparable universe. If compared to the mean enterprise value of this comparable universe, the discount of Zafgen shares is more significant at 70%.

Exhibit 11: Zafgen Comparable Company Analysis

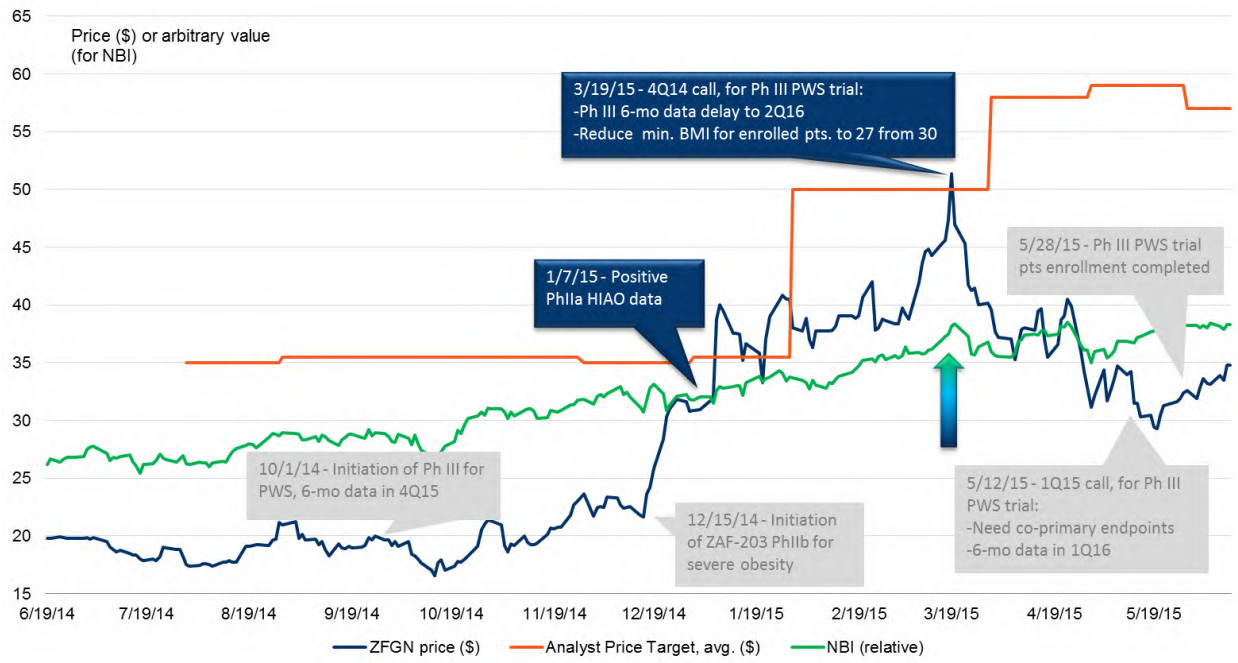
Company	Ticker	Enterprise Value ($MM)	Price 6/15/2015	Shares Out (MM)	Market Cap ($MM)	Cash ($MM)	Debt ($MM)	Stage of Most Advanced Asset
Corcept Therapeutics Incorporated.	CORT	679.2	6.5	107.8	695.0	38.0	22.1	Marketed
Aegerion Pharmaceuticals, Inc.	AEGR	703.5	18.4	28.6	526.6	67.4	244.3	Marketed
Synageva BioPharma Corp.	GEVA	7,671.3	225.5	37.2	8,381.9	710.6	0.0	Phase III
Amicus Therapeutics, Inc.	FOLD	1,210.3	14.0	96.4	1,349.9	148.8	9.2	Phase III
Ultragenyx Pharmaceutical, Inc.	RARE	2,839.5	88.7	35.9	3,183.2	343.6	0.0	Phase II
Raptor Pharmaceutical Corp.	RPTP	1,144.6	14.6	80.5	1,172.6	136.0	108.0	Marketed
Mean		**2,374.7**			**2,551.5**			
Median		**1,177.4**			**1,261.2**			
Zafgen	**ZFGN**	**723.2**	35.6	26.9	**957.4**	234.2	0.0	Phase III

Source: SunTrust Robinson Humphrey, FactSet

Our PT of $47 for Zafgen shares is lower than the Street mean of ~$56. We are bullish on shares of Zafgen as reflected by the 32% premium of our PT over the current Zafgen share price. We believe our $47 PT is justifiable based on our various financial models and perhaps more intuitive after drawing information from key events having occurred at Zafgen and correlating with the history of PT changes on Zafgen shares.

According to the PT history demonstrated in the exhibit below, there were two waves of PT increases from the initial PT of ~$35 post IPO: one was the increase of the average PT to ~$50 upon the release of positive Phase IIa HIAO data on January 7th, 2015, and the second wave was the increase to ~$58 post the 4Q14 earnings call on March 19, 2015. We believe the first wave of PT increases to ~$50 upon positive HIAO data is certainly justifiable. However, we feel that the second wave of PT increases to the current average PT of $56 might be a passive response to the continued increase of Zafgen's stock price and the boom of the overall biotech space as reflected in the rally of the NASDAQ Biotechnology Index (NBI), and therefore it may not be quite as justifiable.

Exhibit 12: Zafgen Stock Price, Key Events, and Analyst Average Price Target



Note: NASDAQ Biotechnology Index (NBI) values are divided by 100 to show relative values
Source: FactSet, Zafgen public filings and press releases, SunTrust Robinson Humphrey

We believe what was announced on the 4Q14 call, including the delay by six-months of the Phase III PWS trial to 2Q16 and the reduction of minimum BMI for enrolled patients to 27kg/m^2 from 30kg/m^2 , were incrementally negative to ZFGN shares. Additionally the requirement of co-primary endpoints for the ongoing Phase III PWS trial announced on the 1Q15 call we believe created increased uncertainty for the probability of success for the trial. Therefore, while bullish near-term on the prospects of Zafgen, we believe our metrics are more realistically tempered than the Street's estimates at this time-point.

Overall, we believe Zafgen is a differentiated Orphan obesity play with the potential to address the much larger obesity and NASH markets. We remain steadfast with our $47 PT for Zafgen shares and believe there is significant upside potential for investors.

Investment Risks

The primary risks associated with an investment in Zafgen include the following:

Clinical risk: While beloranib has accumulated consistent and promising data over the six completed clinical trials and we believe beloranib has a high likelihood of success in the ongoing ZAF-311 Phase III bestPWS trial for the treatment of PWS; there is no guarantee of success. The change in trial duration and dosage, and the employment of co-primary endpoints as compared to the ZAF-211 Phase IIa trial, are uncertainties.

Regulatory risk: Despite the promising data from clinical trials to date, there is no guarantee that future clinical trials will also be successful and that the FDA will approve beloranib. The FDA's requirement of co-primary endpoints should raise the bar for approval; but the Agency lowered the bar by reducing the required level of statistical significance to p <0.05 from p <0.025, which net-net could potentially increase or decrease the bar for approval. Our understanding is that the FDA has not signed off as to the required level of weight reduction as compared to placebo in the Phase III ZAF-311 trial, which could be an uncertainty.

Commercial risk: Zafgen has not previously launched or marketed a commercial product. In order to successfully commercialize beloranib, Zafgen needs to establish a salesforce as well as secure payer coverage for beloranib. The formulary decision is based on not only the clinical data, but also on the pricing of beloranib among other factors, which are currently unknown variables. Should beloranib fail to be covered, we expect it will significantly diminish beloranib's commercial prospects.

Beloranib for PWS (Prader-Willi Syndrome)

PWS is a Rare Genetic Disease That Causes Obesity

PWS is a rare genetic disorder caused by abnormalities on chromosome 15. Behavioral and metabolic symptoms associated with PWS are partially due to defects in the hypothalamus, a portion of the brain that links the nervous system to the endocrine system. The hypothalamus controls the body's sense of hunger, fat metabolism as well as other important functions. The pathophysiology associated with hypothalamic and pituitary dysfunction often is associated with an increased sense of hunger, short stature, central obesity, hypogonadism, and osteoporosis.

Published population studies estimate the prevalence of PWS in the U.S. at between 1:16,000 and 1:25,000, and in the EU at 1:8,000 to 1:50,000. Orphanet, a reference portal for information on rare diseases and Orphan drugs, estimates the prevalence of PWS to be between one and nine per 100,000 people and affecting approximately 1:25,000 births.

Most PWS patients are diagnosed in infancy due to hypotonia (low muscle tone and reduced muscle strength). The increasing popularity of newborn screening also aids in the diagnosis of PWS in neonates. Our pediatric endocrinology consultant believes that over 50% of PWS patients are diagnosed at birth and 90% of PWS patients are diagnosed during their lifetime.

Zafgen and our consultants estimate that approximately 50% of PWS patients are 12 years of age or older, which is the PWS population Zafgen is actively enrolling in the ongoing ZAF-311 Phase III trial. The average life expectancy is 32 years of age for PWS patients, and survival after 50 years of age is uncommon without the assistance of caregivers, primarily due to obesity caused by over-eating and metabolic complications, including cardiovascular disease, diabetes, and sleep apnea.

Hyperphagia which is an abnormally increased appetite for food, and obesity, are the most distinctive and concerning issues for PWS patients.

Exhibit 13: PWS Patients: 16 Months of Age and 18 years of Age

Source: National Institutes for Health

PWS has been classically described as having two major phases: 1) poor feeding and 2) onset of hyperphagia leading to obesity. Phase 1 occurs from birth to early infancy when PWS infants have hypotonia and a poor ability to suckle which often results in the need for tube feeding. Phase 2 begins between one and six years of age. The stages of PWS in a patient's life have different clinical manifestations, as detailed below.

Infancy — Severe hypotonia, poor suckling, and feeding difficulties without a clear underlying cause are the most prominent symptoms for PWS and warrants genetic testing to rule out or confirm PWS.

Childhood — Most PWS patients have growth hormone deficiency. Children with PWS demonstrate delayed development in motor milestones, short stature, symptoms of hyperphagia and obesity if access to food is unrestricted, increased fat mass, and decreased lean mass.

Adolescence and Adulthood — Secondary sexual characteristics generally are delayed or are incomplete in PWS patients at the adolescent stage. Obesity and hyperphagia behaviors are common in PWS patients. Our consultants and the medical literature suggest that approximately 80% of adult PWS patients and approximately 50% of pediatric PWS patients are obese. Adolescent and adult PWS patients often present with complications associated with obesity (including diabetes, sleep apnea, and atherosclerosis), hypogonadism, and behavioral issues related to hyperphagia. Behavioral problems, including temper tantrums, stubbornness, obsessive-compulsive behaviors and skin picking are common issues in PWS patients.

The Most Concerning Symptoms of PWS are Hyperphagia and Obesity

PWS children between the ages of one and six years often start to manifest symptoms of hyperphagia and obesity. As PWS patients grow into adolescence and adulthood, they become more independent and tend to have less-restricted access to food, and therefore obesity resulting from hyperphagia and overeating is more frequently observed. Due to neuroanatomical abnormalities in the hypothalamus among other causes, PWS patients do not experience the normal feeling of satiety after food intake, have a reduced inclination for nausea and vomiting, and have slower metabolisms and suffer from hypersomnolence. If food intake is not properly managed and restricted, obesity develops.

Obesity related co-morbidities are the most frequent causes of death in PWS patients. Diseases resulting from obesity include cardio-respiratory failure, apnea, septicemia due to skin infections, and

pneumonia. Epidemiological surveys have emphasized the risks of choking (8% of deaths) due to the rapid consumption of food, and gastric necrosis and rupture (2% of deaths) from overeating.

Hyperphagia and associated behaviors not only lead to overeating and obesity, but also impair a PWS patient's ability to live independently, to work in conventional workplaces, and to engage in normal social activities. Hyperphagia in PWS patients tend to lead to unusual food-related behaviors, including sneaking and stealing food, seeking food in trash, getting up at night to seek food, and eating items not fit for human consumption (e.g., animal food, spoiled food, decorative items that look like food, garbage, etc.)

A small proportion of PWS patients, less than 10% according to our consultant, live in group homes which are specialized living facilities with skilled and trained supervisors to help guide PWS patients. PWS patients in these settings tend to be less obese and have longer life expectancies. However, the majority of PWS patients reside with their families that undertake the effort to supervise and prevent overeating by placing locks and alarms on cabinets and refrigerators.

Our pediatric endocrinology consultant noted that a reduction in hyperphagia associated behavior could be clinically meaningful for PWS patients as this could potentially enable patients to live independently or even attend school or work. Additionally our physician expert emphasized that with regard to the co-primary endpoints employed in Zafgen's Phase III clinical trials for PWS either weight loss or improvement of hyperphagia related behaviors could be clinically meaningful and they would prescribe the drug if approved with improvement in either of these co-primary endpoints.

An Unmet Medical Need Exists for PWS

Current clinical management of PWS includes the treatment of the aforementioned symptoms. Although there are therapeutics, including human growth hormone (Pfizer's Genotropin (somatropin) rhGH approved for PWS in 2000), for PWS patients that have growth hormone deficiency, there are currently no FDA approved drugs to treat the conditions of obesity or hyperphagia associated with PWS. We believe there is significant unmet medical need in treating PWS. Treatments currently employed by physicians are as follows:

Hyperphagia behavior control: Control of hyperphagia behavior centers on methods to limit the access to food (e.g., locks on cabinets and refrigerators), and to limit exposure that allows the patient to perseverate on food. Bariatric surgeries have not been shown to reduce hyperphagia or achieve long-term weight reduction and are associated with an increased morbidity and mortality. Our consultants note that bariatric surgeries are rarely used for PWS patients.

Obesity control: Strict limitation of food intake is the basis of obesity management in PWS patients. Pharmacotherapy has not been successful. Anorectic agents such as phentermine (one component of the obesity drug Qsymia) and fenfluramine are ineffective in controlling appetite in PWS patients. Selective serotonin reuptake inhibitors (SSRIs) could be effective for the behavioral symptoms in PWS patients, but little evidence exists that demonstrate these drugs have an effect on binge eating, hyperphagia, or weight gain. Topiramate (the other component of Qsymia) does not decrease caloric consumption, BMI, or self-reported appetite in an eight-week open-label trial conducted in eight adult PWS patients.

Although there are no published studies, we believe that recently approved obesity drugs, including Qsymia, Belviq, and Contrave, may not be effective for the treatment of PWS and HIAO. These

drugs all target the hypothalamus, however most patients suffering from PWS or HIAO have impairments in the function of the hypothalamus. Saxenda, works peripherally by stimulating the expression of GLP-1 (Glucagon-like Peptide 1), which might be modestly effective. But no clinical trials have been conducted for the treatment of PWS or HIAO.

Type 2 diabetes management: Type 2 diabetes is present in approximately 25% of adult PWS patients with a mean onset of 20 years of age. It is recommended to prescribe diabetic management protocols and to use pharmacological agents as with non-PWS obesity-related diabetes, including metformin, thiazolidinediones, and/or insulin, to manage Type 2 diabetes in PWS patients.

Growth hormone (GH) insufficiency management: GH insufficiency is prevalent in PWS patients which leads to reduced growth velocity. GH for children with growth failure and genetically confirmed PWS was approved in the U.S. and EU in 2000. It has been shown that GH improves lean mass, motor development, and normalization of body habitus. The safety associated with GH treatment however, could be a concern as several deaths in PWS children treated to GH have been reported. The deaths were associated with respiratory problems occurring within the first three months of GH treatment. Several risk factors, including severe obesity, sleep apnea, and respiratory infection, may contribute to GH-associated mortality. One of our consultants noted that early treatment with GH in pediatric patients could potentially reduce hyperphagia behavior and obesity. However, another expert and the medical literature suggest that the effects of GH in reducing body fat in pediatric patients may be transient in nature, and has a minimal effect on BMI.

Despite the availability of methods to manage certain PWS symptoms, we believe they fail to sufficiently address two major aspects of PWS: hyperphagia and obesity. As a result, a significant unmet medical need continues to exist for patients suffering from PWS.

Diagnosis is Straightforward and Most Patients are Diagnosed at an Early Age

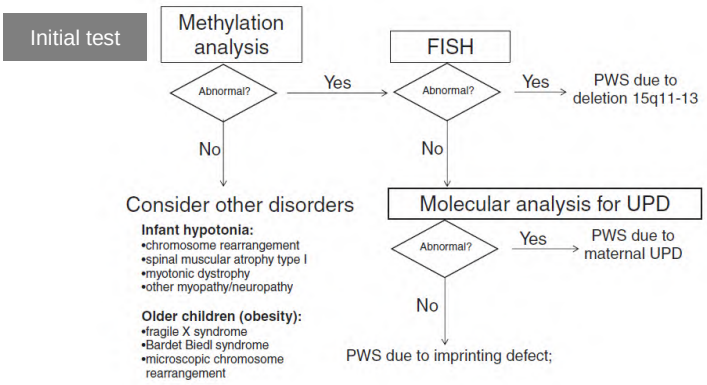
PWS is often diagnosed at a young age due to the presence of hypotonia as well as other symptoms. Patients suspected of having PWS have characteristic clinical features and the diagnosis is confirmed through genetic testing. Clinical diagnostic criteria were developed in 1993. For children three years of age or younger, a diagnosis of PWS is likely if five points are scored from among the criteria that follow (four from major criteria); for children older than three years of age or for adults, eight points are required (five or more from among the major criteria).

- Major criteria (1 point each): infantile hypotonia, feeding problems, excessive weight gain after infancy, characteristic facial features, hypogonadism, global developmental delay, hyperphagia.
- Minor criteria (0.5 point each): decreased fetal movement, characteristic behavior problems, sleep disturbances or sleep apnea, short stature, hypo-pigmentation, small hands and/or feet, narrow hands with straight ulnar border, eye abnormalities (esotropia, myopia), thick viscous saliva with crusting at the corners of the mouth, speech articulation defects, skin picking.

As PWS is caused by genetic defects, i.e., absence of expression of the paternally active genes on the long arm of chromosome 15, either due to deletions from the paternal chromosome, maternal disomy, or rarely defects in the imprinting center, molecular testing can be employed to definitively confirm PWS, which is highly sensitive (>99% sensitivity). A standard PWS diagnostic panel begins

with karyotype and methylation tests, followed by fluorescence *in-situ* hybridization (FISH), and then microsatellite probes to detect maternal uniparental disomy (UPD).

Exhibit 14: PWS Genetic Testing Algorithm



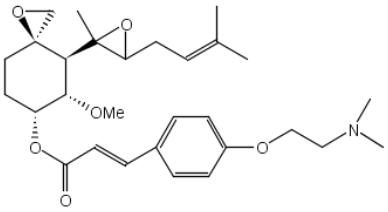
Source: SunTrust Robinson Humphrey adapted from Pediatrics. 2011 Jan;127(1):195-204.

Based on a high diagnoses rate for PWS and a significant unmet medical need, we estimate a potentially high treatment rate, a swift adoption, and premium pricing if a pharmacotherapy, such as Zafgen's beloranib, is approved and becomes commercially available. Based on our revenue build-up model for beloranib, we expect peak sales booked by Zafgen for beloranib in PWS of ~$950 million in the year 2024.

Beloranib Targets PWS via a Unique Mechanism of Action Modulating Different Molecular Pathways

Zafgen is developing beloranib, an inhibitor for methionine aminopeptidase 2 (MetAP2) that modulates the activity of key cellular processes controlling metabolism, for the treatment of PWS as well as other Orphan obesity diseases as well as broader metabolic indications.

Exhibit 15: The Chemical Structure of Beloranib



Source: SunTrust Robinson Humphrey

Beloranib is a first-in-class small molecule with a mechanism of action (MOA) that combines the effects of both hunger reduction and fat utilization. Beloranib is the first anti-obesity agent with the potential to address appetite control and energy consumption by targeting different systems of the body. We believe this MOA is different from previously approved obesity drugs.

Exhibit 16: MOA and Target Organ of Beloranib and Other Anti-Obesity Agents

Drug	Mechanism of Action	Target System
Approved		
Phentermine	Noradrenaline releaser, sympathomimetic	CNS
Alli/Xenical (orlistat)	Gastric and pancreatic lipase inhibitor	GI
Belviq (lorcaserin)	5HT2C receptor agonist	CNS
Qsymia (phentermine and topiramate)	Noradrenaline releaser and anti-convulsant	CNS
Contrave (naltrexone and bupropion)	Opioid receptor antagonist/noradrenaline/dopamine reuptake inhibitor	CNS
Saxenda (liraglutide)	GLP-1 receptor agonist	GI
In Clinical Development		
Empatic (bupropion with zonisamide)	Noradrenaline/dopamine reuptake inhibitor and anti-	CNS
Tesofensine	Serotonin/noradrenaline/dopamine reuptake inhibitor	CNS
Cetilistat	Pancreatic lipase inhibitor	GI
Beloranib	**MetAP2 inhibitor**	**CNS+liver+adipocyte**
Velneperit	Neuropeptide Y5 receptor antagonist	CNS
rm-493	Selective peptide agonist for the melanocortin 4 receptor	CNS
Pramlintide	Analog of amylin	GI
TT-401	Glucagon/GLP-1 dual agonist	GI
PP1420	Pancreatic polypeptide analog	GI
GSK 598809	D3 (dopamine) antagonist	CNS
ZP-2929	Glucagon/GLP-1 dual agonist	GI
Withdrawn from Market		
Fen-Phen (fenfluramine/phentermine)	Serotonin/noradrenalin releasers	CNS
Rimonabant	CB1 receptor antagonist	CNS
Sibutramine	Serotonin/noradrenalin reuptake inhibitor	CNS

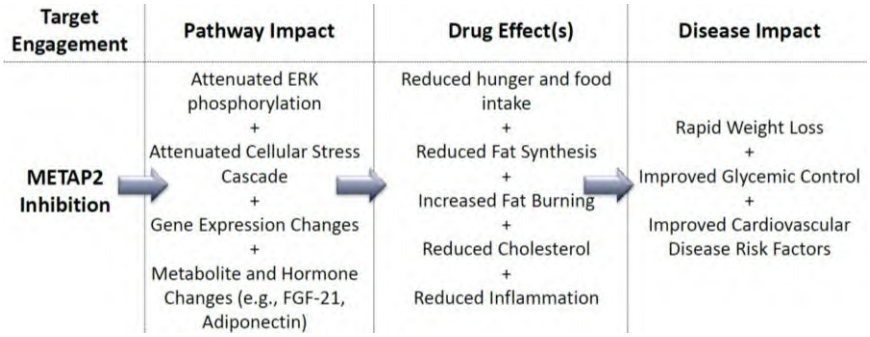
Source: SunTrust Robinson Humphrey adapted from Diabetes Metab Syndr Obes. 2014; 7: 73–84. and Trends Neurosci. 2013 Feb;36(2):133-40.

Beloranib binds and inhibits its molecular target, MetAP2, which suppresses the lipid synthesis pathway in the liver and decreases fat storage throughout the body. The reduction of newly synthesized fatty acids by the liver drives the conversion of stored fats into energy to maintain homeostasis, while reducing hunger.

MetAPs are a class of enzyme with biological functions that remove methionine from the amino-terminus of newly synthesized proteins, which is important for further amino terminal modifications (e.g., acetylation) as well as for protein stability. It has been found that the increased expression of the *METAP2* gene is associated with various forms of cancer, including colon cancer, and that MetAP2 may induce tumor growth by promoting angiogenesis (the formation of new blood vessels). Due to MetAP2's potential role in oncogenesis, MetAP2 inhibitors were first developed as anti-cancer agents. However, it was also observed that MetAP2 inhibitors also induced sustained weight reduction in animal models, which was the genesis of developing MetAP2 inhibitor to treat obesity.

The precise MOA for the anti-obesity effect of MetAP2 inhibitors, including beloranib, has not been fully elucidated. Current understanding suggests that beloranib suppresses phosphorylation and activation of extracellular signal-regulated kinases 1 and 2 (ERK1/2). Beloranib then inhibits sterol regulatory element binding protein (SREBP) activity via ERK-related pathways, leading to reduced lipid and cholesterol biosynthesis and increased beta oxidation of fatty acids. Beloranib may potentially lead to a change in the expression of metabolites and hormones, including fibroblast growth factor-21 (FGF-21), and factors related to inflammation. Our conversations with physician experts confirm a lack of full understanding of the MOA for beloranib and other MetAP2 inhibitors. However, clinical data should be of greater importance when treating PWS and HIAO patients in real clinical practice.

Exhibit 17: Mechanism of Action of MetAP2 Inhibitors and the Impact on Obesity



Source: Zafgen public filings, SunTrust Robinson Humphrey

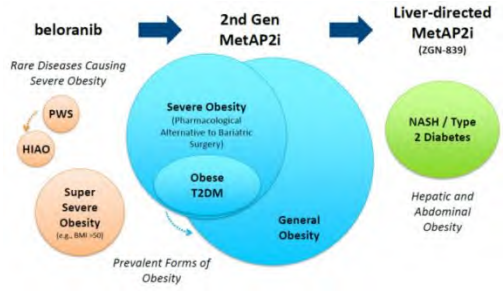
Beloranib received Orphan Drug Designation for the treatment of PWS in both U.S. and EU in January 2013 and July 2014, respectively. Zafgen is also pursuing Orphan Drug Designation for beloranib in HIAO in the U.S. and EU.

PWS is Not the Whole Story; HIAO and Other Indications are to Follow

Zafgen intends to target PWS as the lead indication for beloranib. However, PWS is only the first indication in Zafgen's corporate strategy, which includes the advancement of beloranib in Orphan diseases where obesity is a co-morbidity of an underlying condition, including PWS, HIAO and monogenic loss of function mutations (e.g., leptin deficiency and melanocortin receptor subclass 4 mutations). The focus on Orphan diseases such as PWS and HIAO allows Zafgen to rapidly develop beloranib using smaller and less costly clinical trials, to charge a premium price after regulatory approval, and to potentially obtain broader payer coverage.

Following the Orphan obesity indications, Zafgen intends to develop second generation MetAP2 inhibitors for the treatment of more prevalent metabolic diseases associated with a much larger patient population, including general obesity of varying severity, and nonalcoholic steatohepatitis (NASH).

Exhibit 18: Zafgen Corporate Strategy



Note: size of bubble represents relative size of patient population; Source: SunTrust Robinson Humphrey adapted from Zafgen public presentation

Clinical Development

A total of over 250 patients have been treated in six different clinical trials with beloranib to date. A wide range of doses (0.2mg to 6.0mg) has been examined for varying durations (four to 12 weeks) with different administrations and different scheduling parameters (IV BIW, IV QW, and SubQ BIW). The reliance on this previous data is central to Zafgen's Phase III development strategy for beloranib and for investor confidence in the Phase III program as well.

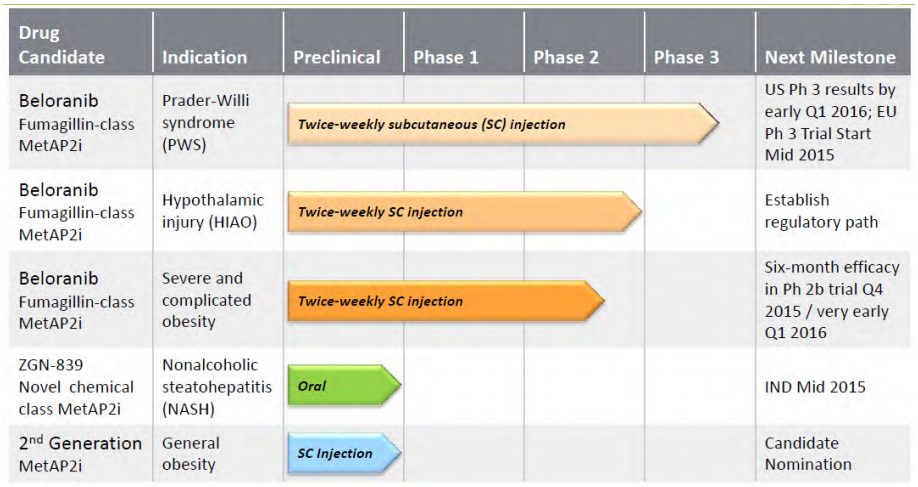
Exhibit 19: Zafgen Ongoing and Completed Clinical Trials for Beloranib

Trial Name	Phase	Indication	Trial Type	Dosing Regimen	Treatment	Pts Number	BMI (kg/m^2)
Completed Trials							
ZAF-001	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• Escalating doses of 0.1mg/m^2, 0.3mg/m^2, and 0.9mg/m^2, or ~0.2mg, 0.6mg, and 2mg • IV BIW	4 weeks	31 (all female)	32-45
ZAF-003	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• 3.0mg, 6.0mg, and 2.5mg • 3.0mg and 6.0mg given IV BIW for 4 weeks • 2.5mg given IV BIW for the 1st week and QW for the subsequent 6 weeks	4 weeks or 7 weeks	25 (all female)	30-50
ZAF-101	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• 1.0mg, 2.0mg, and 4.0mg • SubQ BIW	4 weeks	25 (all female)	30-45
ZAF-201	IIa	Severe Obesity	Randomized, DB, Placebo-controlled	• 0.3mg, 0.6mg, 1.2mg, 2.4mg, and 3.2mg • SubQ BIW	12 weeks	160 (157 female)	30-50
ZAF-211	IIa	PWS	Randomized, DB, Placebo-controlled	• 1.2mg and 1.8mg • SubQ BIW	4 weeks	17	26-44
ZAF-221	II	HIAO	Randomized, DB, Placebo-controlled	• 1.8mg • SubQ BIW	4 weeks + 4 weeks extension	14	30-55
Ongoing Trials							
ZAF-203	IIb	Severe Obesity with T2D	Randomized, DB, Placebo-controlled	1.2mg and 1.8mg SubQ BIW	12 months with 6 months interim	150	30-60
ZAF-311 (bestPWS)	III	PWS	Randomized, DB, Placebo-controlled	1.8mg, 2.4mg SubQ BIW	6 months + 6 months open label	102+	Age 12-17: BMI≥ 95th percentile for age and gender, Age 18+: BMI 27-60

Note: DB, double blind; Source: Zafgen public filings, SunTrust Robinson Humphrey

Zafgen's development and commercial strategy encompasses the advancement of multiple clinical programs in targeting rare obesity indications as well as indications affecting a broader population, such as general obesity and nonalcoholic steatohepatitis (NASH).

Exhibit 20: Zafgen Clinical Development Plan



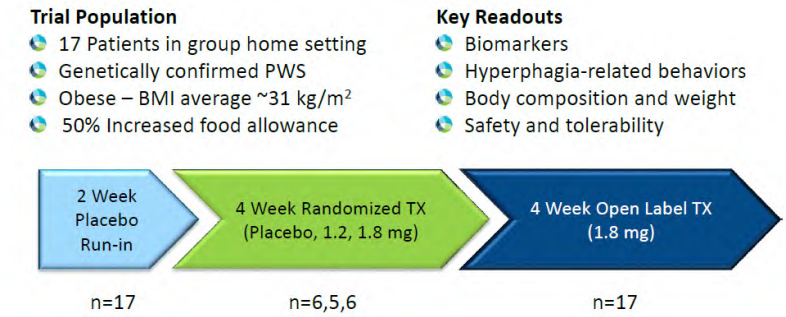
Source: Zafgen public presentation

ZAF-211 Phase IIa Trial

Trial Design and Background Information

In January 2014, Zafgen announced top-line results from a Phase IIa clinical trial for beloranib in treating patients with PWS. This was a randomized, double-blind, placebo-controlled clinical trial evaluating 1.2mg and 1.8mg doses of beloranib as compared to placebo in 17 adult patients (mean age of 33.5 years) with all PWS patients living in closely-controlled PWS-specific group homes.

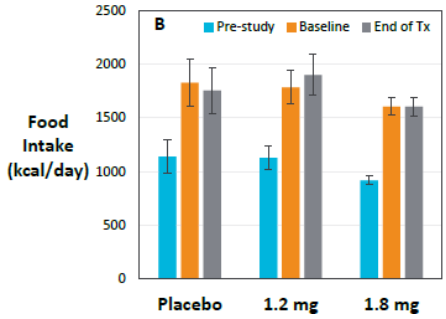
Exhibit 21: ZAF-211 Phase IIa Clinical Trial Design



Source: Zafgen public presentation

All patients started with a two-week single-blind placebo lead-in period, followed by a four-week double-blind randomized treatment period, at the end of which an optional four-week open-label extension phase with 1.8mg beloranib being offered to patients. During the course of the trial daily calorie allowances were increased by 50% to drive modest weight gain and simulate the greater access to food experienced in the general PWS population living in family-home situations. As demonstrated in the following exhibit, food intake increased in all three arms as compared to respective pre-study levels (orange and gray vs. blue). Treatment with beloranib did not appear to change food intake (grey vs. orange). The reason for a lack of effect of beloranib in suppressing food intake is that these PWS patients were previously on a restricted diet with calorie allowance of approximately 1,000kcal/day. For an average person of 30 to 40 years of age and moderate activity, the average daily caloric intake is between 2,000kcal/day and 3,000kcal/day. Therefore, even with a 50% increase in calorie allowance, these PWS patients were still below average in caloric consumption compared to the general population, and thus likely to consume all of the food provided to them.

Exhibit 22: Food Intake Levels in the ZAF-211 Phase IIa Trial



Source: Zafgen reported data

Primary and second endpoints of the trial were as follows:

Primary endpoint:

- Percent change in body weight from baseline at the end of the randomized dosing period

Secondary endpoints:

- Change in body weight (kg) from baseline to the end of the randomized dosing period

- Change in hyperphagia behavior, drive, and severity score (total score) from baseline to the end of the randomized dosing period using the PWS Hyperphagia Questionnaire (PWS-HQ)

PWS-HQ was used to assess PWS phenotype as recorded by a caregiver who measured the frequency and severity of behavioral issues typical in patients with PWS. Zafgen slightly modified the questionnaire by removing one question in the ongoing Phase III ZAF-311 PWS trial at the FDA's request, which we will discuss later in this report. As detailed in the Exhibit, PWS-HQ is comprised of 10 questions that address three aspects of PWS phenotypes: behavior, drive and severity. A score of 0 to 4 is assigned to each of the questions which results in a summed total score of 0 to 40.

Exhibit 23: Dykens Hyperphagia-Related Behavior Score Questions and Categories

Sub-score	Questions – "During the past 2 weeks…" (scale of 0 to 4 for each question)
Behavior	● How often did the person try to bargain or manipulate to get more food at meals? ● How often did the person forage through the trash for food? ● How often did the person get up at night to food seek? ● How often did the person try to steal food (that you are aware of)?
Drive	● How upset did the person generally become when denied a desired food? ● Once the person had food on their mind, how much effort did it take for you or others to redirect him/her away from food to other things?*
Severity	● How persistent was the person in asking or looking for food after being told "no" or "no more"? ● When others tried to stop the person from talking about food, how distressed did he or she generally ● Outside of normal meal times, how much time did the person generally spend talking about food? ● How often did food-related talk or behavior interfere with the person's normal daily activities, such as self-care, recreation, school, or work?

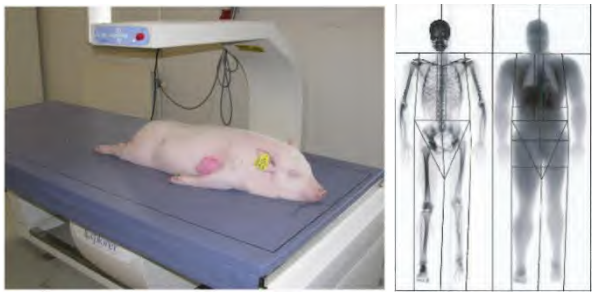
*Note: *Question has been removed for Phase III studies following FDA feedback*
Source: Zafgen public presentation, SunTrust Robinson Humphrey

The current 10-question PWS-HQ was modified from the questionnaire originally published by Dr. Elisabeth M. Dykens of the Vanderbilt University in a paper in the journal Obesity in 2007 that contained 13 questions.

In addition to body weight and PWS-HQ, the trial also assessed the effect of beloranib on the change in body mass and fat content by employing dual-energy x-ray absorptiometry (DEXA) scan analysis and responses in metabolic biomarkers.

DEXA employs two X-ray beams with different energy levels to assess body composition. The scan is used primarily to evaluate bone mineral density but can also be used to measure total body composition and fat content.

Exhibit 24: Illustration of a DEXA Machine and Scan Result



Source: National Institutes of Health

PWS patients were relatively well distributed among the three arms. However, patients in the 1.8mg beloranib arm had worse disease manifestations with regard to weight, BMI, hyperphagia questionnaire total score, and total fat mass.

Exhibit 25: ZAF-211 Baseline Patient Characteristics

		Beloranib	
Characteristic (mean (SD) or number (%))	**Placebo (N=6)**	**1.2mg (N=5)**	**1.8mg (N=6)**
Female, n (%)	3 (50.0)	4 (80.0)	4 (66.7)
Age, years	32.5 (4.8)	37.2 (10.8)	31.5 (9.8)
Weight, kg	69.9 (16.7)	66.4 (9.6)	78.2 (15.3)
BMI, kg/m^2	29.8 (5.3)	29.4 (3.4)	34.7 (5.8)
Confirmed diagnosis of PWS			
Uniparental disomy	3 (50.0)	1 (20.0)	2 (33.3)
Chromosome 15 microdeletion	3 (50.0)	4 (80.0)	4 (66.7)
Hyperphagia Questionnaire Total Score	8.2 (9.2)	7.5 (6.1)	12.5 (5.8)
Pre-study daily caloric allowance	1142 (388)	1130 (254)	917 (98)
Adiponectin, mg/mL	6.2 (4.4)	6.6 (2.5)	4.8 (1.8)
hsCRP (mcg/mL)	2.5 (1.9)	3.1 (3.8)	1.4 (0.9)
Leptin, ng/mL	16.1 (5.1)	27.6 (11.3)	32.0 (13.5)
HDL cholesterol, mmol/L	1.1 (0.3)	1.4 (0.3)	1.1 (0.2)
LDL cholesterol, mmol/L	2.3 (0.8)	2.1 (0.7)	2.5 (0.9)
Total cholesterol, mmol/L	3.8 (0.8)	4.1 (0.5)	4.0 (1.1)
Triglycerides, mmol/L	2.4 (1.2)	1.9 (0.7)	2.0 (0.7)
Total body mass, kg	69.7 (15.3)	65.5 (9.6)	77.7 (15.5)
Total body fat mass (DEXA), kg	31.1 (9.2)	29.5 (7.2)	39.0 (9.9)
Total body lean mass (DEXA), kg	36.2 (7.8)	34.1 (2.9)	36.3 (7.9)

Source: Zafgen reported data, SunTrust Robinson Humphrey

Efficacy in Body Weight and Body/Fat Mass

Key results are summarized in the exhibit that follows. Patients from both doses of beloranib were combined into one group for data analysis, according to a pre-specified statistical analysis:

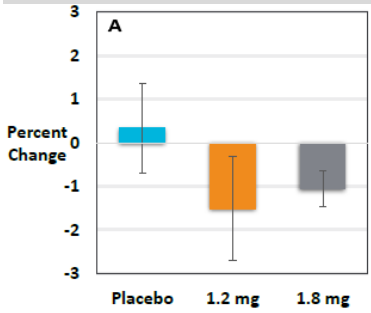
Exhibit 26: ZAF-211 Phase IIa Trial Results

	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	-1.3	0.17*
Body mass (kg) (DEXA)	69.7	2	72.1	-2.1	0.002
Fat mass (kg) (DEXA)	31.1	3.6	34.6	-2.9	0.013

*Note: *not statistically significant by ANCOVA, a pre-specified statistical analysis, used to assess changes in all key endpoints;*
Source: Zafgen public filings, SunTrust Robinson Humphrey

When examining the individual doses, both the 1.2mg and 1.8mg beloranib doses demonstrated a trend in decreasing body weight as compared to placebo. However, the 1.2mg arm appeared to have a more profound reduction.

Exhibit 27: Change in Body Weight in the ZAF-211 Phase IIa Trial



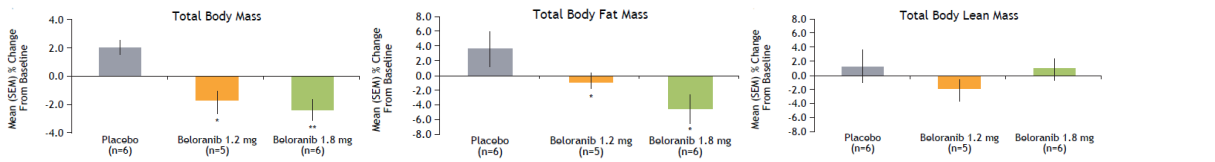
Source: Zafgen reported data, SunTrust Robinson Humphrey

Management noted that the reason for a lack of dose-dependent effect and a high data variation observed in the weight reduction results were primarily due to patient compliance issues. In the Phase IIa trial all PWS patients live at PWS group homes which were a less familiar and comfortable environment as compared to PWS patients staying at home with parents and family. This could result in emotional instability in these PWS patients that often have baseline behavioral problems, including temper tantrums, stubbornness, and obsessive-compulsive behavior. They may be non-compliant during the process of weighing-in. Management noted that some patients were weighed with shoes/clothes off, but some with shoes/clothes on; some patients had extra items, such as chicken wings, in their pockets when they were weighed. These factors, we believe, would skew the results. According to management these variables will be addressed in the ongoing Phase III trials. One method is to limit the time PWS patients stay at group homes to less than 50% so that the

enrolled PWS patients would be more emotionally comfortable and therefore more compliant with the trial protocol.

With regard to body mass, both doses demonstrated a dose-dependent and statistically significant decrease in total body mass as well as whole body fat mass, as assessed by DEXA.

Exhibit 28: Change in Body Mass in the ZAF-211 Phase IIa Trial

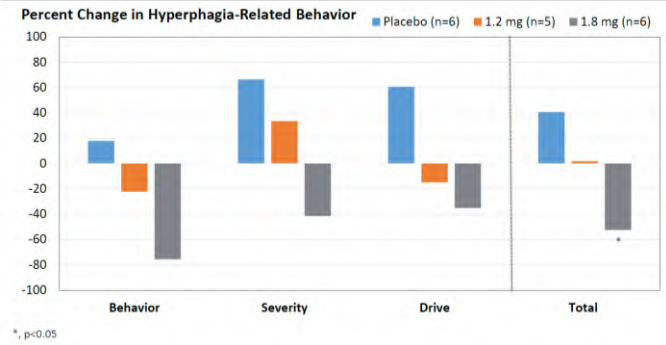


Source: Zafgen reported data

Efficacy in Hyperphagia Behavior

Total PWS-HQ score was reduced by an average of 52.4% in the 1.8mg beloranib arm, as compared to an average increase of 40.5% in placebo and an average increase of 1.8% in the 1.2mg beloranib arm. Statistical analysis via analysis of covariance (ANCOVA) did not demonstrate statistical significance due to the small sample size. However, the comparison of the 1.8mg beloranib arm vs. placebo achieved statistical significance with p =0.025 when assessed by a *post hoc* paired *t*-test. In each of the three categories of PWS-HQ, there was a dose-dependent improvement of these matrices treated with beloranib as compared to placebo. ANCOVA is employed if you want to statistically control for a confounding continuous variable that could explain your result and a paired t-test is employed when you are comparing the mean of two groups two-times in succession (pre- vs post-intervention).

Exhibit 29: Change in PWS-HQ Scores in the ZAF-211 Phase IIa Trial



Source: Zafgen reported data

Efficacy in Cardio-Metabolic Biomarkers

In the exhibit that follows that assesses mean changes in cardio-metabolic parameters from baseline to day 43, beloranib demonstrated a statistically significant increase in the metabolic beneficial biomarker adiponectin (by over 75%) and HDL-cholesterol (by over 20%), as well as a decrease in LDL (by over 20%). Our consultants noted that the panel of results looked promising.

Exhibit 30: Mean Changes from Baseline To Day 43 For Cardiometabolic Parameters

	Placebo (N=6)	Beloranib 1.2mg (N=5)	Beloranib 1.8mg (N=6)
Adiponectin (µg/mL)			
Baseline	6.22	6.62	4.78
LS Mean Change	-0.12	5.04	4.58
p -value vs. placebo		<0.001	0.001
hs-CRP (µg/mL)			
Baseline	2.46	3.09	1.44
LS Mean Change	1.52	0.63	-1.8
p -value vs. placebo		0.537	0.03
Leptin (ng/mL)			
Baseline	16.13	27.6	32
LS Mean Change	-2.72	-9.91	-12.82
p -value vs. placebo		0.075	0.028
HDL-cholesterol (mmol/mL)			
Baseline	1.13	1.44	1.13
LS Mean Change	-0.01	0.38	0.26
p -value vs. placebo		0.008	0.028
LDL-cholesterol (mmol/mL)			
Baseline	2.3	2.14	2.47
LS Mean Change	0.05	-0.51	-0.77
p -value vs. placebo		0.037	0.005
Total cholesterol (mmol/mL)			
Baseline	3.78	4.1	3.98
LS Mean Change	-0.11	0	-0.52
p -value vs. placebo		0.624	0.106
Triglyceride (mmol/mL)			
Baseline	2.42	1.9	1.95
LS Mean Change	0.05	-0.19	-0.37
p -value vs. placebo		0.618	0.382

Source: Zafgen reported data, SunTrust Robinson Humphrey

Safety Profile

Both 1.2mg and 1.8mg beloranib doses appeared to be well-tolerated. The rate and severity of treatment-emergent adverse events (TEAEs) was comparable among the three treatment groups. There were no deaths, severe adverse events (SAEs) reported in the clinical trial as related to treatment. No clinically significant changes in laboratory, ECG or vital signs were observed. Injection-site bruising of mild severity was the most common TEAE, which occurred at comparable rates for both the beloranib and placebo arms. Sleep disturbance, a side effect leading to a >50% withdrawal rate in the 2.4mg beloranib arm in the ZAF-201 Phase IIa trial in treating severe obesity, was not observed in this trial, the reason of which will be discussed in the ZAF-201 trial section.

Exhibit 31: ZAF-211 Most Common TEAEs

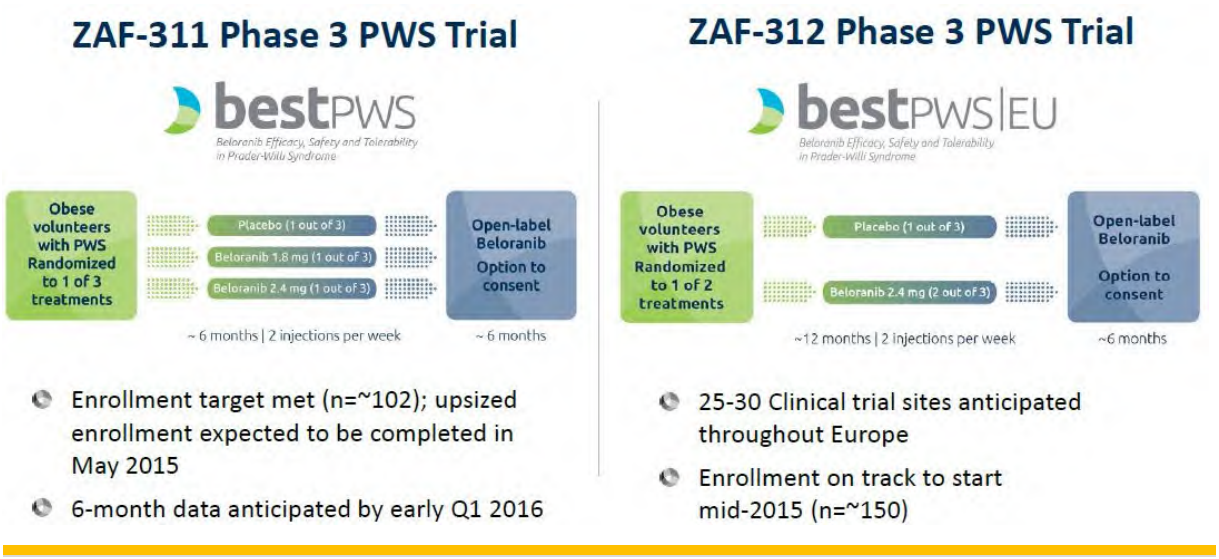
Subjects/Events	1.2 mg (N=5)	1.8 mg (N=6)	Placebo (N=6)
Injection site bruising	2 (40.0%)/2	1 (16.7%)/1	2 (33.3%)/2
Abdominal pain	1 (20.0%)/1	0 / 0	0 / 0
Adrenal insufficiency	1 (20.0%)/1	0 / 0	0 / 0
Contusion	0 / 0	1 (16.7%)/2	0 / 0
Decreased appetite	1 (20.0%)/1	0 / 0	1 (16.7%)/2
Hyperhidrosis	0 / 0	1 (16.7%)/1	0 / 0
Injection site reaction	0 / 0	1 (16.7%)/1	0 / 0
Insomnia	0 / 0	1 (16.7%)/1	0 / 0
Mood altered	1 (20.0%)/1	0 / 0	0 / 0
Musculoskeletal pain	0 / 0	1 (16.7%)/1	0 / 0
N-telopeptide urine increased	1 (20.0%)/1	0 / 0	0 / 0
Nightmare	0 / 0	1 (16.7%)/1	0 / 0
Pruritis	1 (20.0%)/1	0 / 0	0 / 0
Psychotic disorder	1 (20.0%)/1	0 / 0	0 / 0
Pyrexia	1 (20.0%)/1	0 / 0	0 / 0

Note: data are in a format of "subjects (% to total subjects in this trial arm) / events"
Source: Zafgen reported data, SunTrust Robinson Humphrey

ZAF-311 and ZAF-312 Phase III Program

Zafgen initiated the ongoing pivotal Phase III clinical trial ZAF-311 (Beloranib Efficacy Safety and Tolerability in PWS, or bestPWS) in October 2014. Based on discussions with the regulatory agencies, Zafgen expects the pivotal Phase III clinical program to consist of two Phase III trials, one in the U.S. (ZAF-311), and the other in the EU (ZAF-312 or bestPWS | EU).

Exhibit 32: PWS Phase III Clinical Program



Source: Zafgen public presentation

The U.S. ZAF-311 randomized, double-blind trial will evaluate the efficacy, safety and tolerability of 1.8mg and 2.4mg doses of beloranib versus placebo over six months of treatment in 108 patients with PWS. An optional open-label extension will be followed for an additional six months of treatment for those patients who have completed the six-month randomized treatment period and agree to

remain on treatment. The initial enrollment target of 108 patients was met in May 2015 and top-line data are expected in 1Q16.

The EU ZAF-312 trial is similar in design to the U.S. trial in evaluating beloranib at 1.8mg and 2.4mg doses versus placebo. The ZAF-312 trial differs with a 12-month treatment period in approximately 150 patients. This trial will also be followed by an open-label extension study for an additional six months of treatment.

Both trials will be conducted in an outpatient setting, including patients living in family homes and group homes specializing in the care of residents with developmental disabilities. Patients need to live in a family home setting ≥50% of the time, and therefore a group home setting <50%, and have a consistent caregiver to provide input for the assessment of PWS-HQ.

Prior to the 1Q15 conference call conducted in May 2015, Zafgen stated that in order to support an NDA submission to the FDA and an MAA submission to the EMA, the Company must achieve in the Phase III clinical trials a statistical significance of p <0.025 on either of the dual primary endpoints: (i) hyperphagia-related behaviors or (ii) change in body mass. According to the Company, to assess the efficacy of these dual endpoints, each will be evaluated for the treatment effect of beloranib 2.4mg at a significance level of p <0.025. If the comparison between the 2.4mg and placebo is statistically significant for a given endpoint, that endpoint will be evaluated for treatment effect of 1.8mg beloranib at a significance level of p <0.025.

However, in May 2015 the Company announced a modification of the primary endpoints "based on conversations with the FDA." The finalized Phase III plan will evaluate beloranib with co-primary endpoints, both of which have to be met with a statistical significance level of p <0.05. The two components of the co-primary endpoints are hyperphagia-related behaviors as measured by total score of (i) a Hyperphagia Questionnaire (PWS-HQ) and (ii) change in total body weight. Secondary endpoints include change in total body mass, body fat mass, LDL, HDL, and triglycerides.

Hyperphagia-related behaviors will be measured by a slightly modified version of the PWS-HQ that was used in the ZAF-211 Phase IIa trial. One question was removed from the 10-question list, per discussions with the FDA, which is highlighted in the exhibit that follows.

Exhibit 33: PWS-HQ Used In the bestPWS Phase III Trial

Sub-score	Questions – "During the past 2 weeks…" (scale of 0 to 4 for each question)
Behavior	● How often did the person try to bargain or manipulate to get more food at meals?
	● How often did the person forage through the trash for food?
	● How often did the person get up at night to food seek?
	● How often did the person try to steal food (that you are aware of)?
Drive	● How upset did the person generally become when denied a desired food?
	● Once the person had food on their mind, how much effort did it take for you or others to redirect him/her away from food to other things?*
Severity	● How persistent was the person in asking or looking for food after being told "no" or "no more"?
	● When others tried to stop the person from talking about food, how distressed did he or she generally
	● Outside of normal meal times, how much time did the person generally spend talking about food?
	● How often did food-related talk or behavior interfere with the person's normal daily activities, such as self-care, recreation, school, or work?

*Note: *Question has been removed for Phase III studies following FDA feedback;*
Source: Zafgen public presentation, SunTrust Robinson Humphrey

Zafgen has been validating PWS-HQ under guidance from the FDA Study Endpoints and Labeling Development staff, and the Company expects to complete the validation during the course of its Phase III program but prior to a regulatory filing. The PWS-HQ will need to be further validated for use in multiple countries with different native languages in support of the ZAF-312 study. Zafgen noted that scientific advice received from the EMA supported the importance of hyperphagia-related behaviors as a clinically meaningful endpoint for PWS and that this ongoing approach to validate PWS-HQ is acceptable.

Similar to the ZAF-211 Phase IIa trial, body fat mass and total body mass will be assessed in both ZAF-311 and ZAF-312 as secondary endpoints, which is defined as a percentage change in body fat content, or total body mass, as measured by DEXA, from baseline to the end of the randomized period with beloranib treatment compared to a change from baseline to the end of the randomized period in patients treated with placebo.

Key inclusion criteria for the ZAF-311 trial include:

- Genetically confirmed diagnosis of PWS
- Age of at least 12 years but not older than 65 years
- Obese
    - Age 12 to 17: BMI $\geqslant 95^{th}$ percentile for age and gender
    - Age 18 to 65: BMI $\geqslant 27 \leqslant 60$ kg/m^2
- Baseline PWS-HQ score of 13 or greater

Key exclusion criteria include:

- Subjects living in a group home $\geqslant 50\%$ of the time

With regard to time-line, the Company initiated the ZAF-311 trial in the U.S. in October 2014; announced full enrollment of 102 patients in May 2015; and expects top-line data in 1Q16. Zafgen expects to initiate its Phase III ZAF-312 trial in the EU in mid-2015, and may take at least six months to enroll the planned ~150 PWS patients into the trial. Based on this we expect top-line data from the EU trial to be reported in mid-2017.

Comparison between ZAF-211 and ZAF-311 and the Potential Read-Through

The ZAF-211 Phase IIa trial was largely successful, in our opinion, in demonstrating both efficacy and safety. However, several changes in clinical trial design were made in the ongoing ZAF-311 (bestPWS) Phase III trial. In this section we compare the differences and draw conclusions from previously conducted trials to project the potential outcome of the ZAF-311 trial.

There are four major changes in the ZAF-311 trial as compared to the ZAF-211 trial. The changes and associated implications are as follows:

- Change in trial duration to six months (26 weeks) from four weeks ⟶ *Is beloranib's efficacy durable during a six-month period?*
- Change dose volume to 1.8mg and 2.4mg from 1.2mg and 1.8mg ⟶ *Is 2.4mg beloranib tolerable? As the 1.8mg dose was less efficacious than the 1.2mg dose, will the 2.4mg dose be even less efficacious?*

- Change primary endpoints to co-primary endpoints including weight loss and change in hyperphagia-related behavior from a single primary endpoint of weight loss ⟶ *Does this increase or decrease the bar for approval? How impactful is the change?*
- Change of trial size to 108 patients from 17 patients ⟶ *Is the trial sufficiently powered?*

Exhibit 34: Comparison between ZAF-201, ZAF-211 and ZAF-311 Trials

	Study Dessign or Result	ZAF-201	ZAF-211	ZAF-311
Baseline Information	Indication	Severe obesity	PWS	PWS
	Phase	IIa	IIa	III
	Patient Number	160	17	108
	Dosing	•0.3mg, 0.6mg, 1.2mg, 2.4mg, and 3.2mg •SubQ BIW	•1.2mg and 1.8mg •SubQ BIW	•1.8mg, 2.4mg •SubQ BIW
	Treatment Duration	12 weeks	4 weeks	6 months + 6 months open label
	BMI Range	30-50	26-44	27-60
	Baseline age	~48	~35	
	Baseline weight	~101kg	~71kg	
Enrollment Criterial	Co-morbid	May have T2D	/	Obesity
	Other major inclusion criteria	Stable weight past 2 mo	BMI ≥25 Stay at group home under supervision during study Stable body weight past 3 mo	Confirmed genetic diagnosis of Prader-Willi Syndrome
	Major exclusion criteria	Use of weight loss agents in past mo T1D	Use of weight loss agent past 3 mo T1D	Live in a group home ≥ 50% of the time
Efficacy Results	Weight reduction	0.3mg not effective, -10.9kg in 2.4mg group, -6.9kg in 1.2mg group, -5.5kg in t0.6mg group, versus -0.4kg in placebo	•-1.27% (~8.5kg) in beloranib group (pooled analysis of 1.2 and 1.8mg groups) versus +0.34% (~2.4kg) change in placebo •1.2mg arm reduced more body weigth	Co-primary endpoints of weight loss and change in hyperphagia-related behavior
	Change in PWS-HQ	/	Reduction in hyperphagia related behaviors (at 1.8mg dose level only).	Remove one question from PWS-HQ used in ZAF211 Phase IIa trial
	Change in fat mass	/	-2.9% in beloranib group versus +3.6% in placebo	
	LDL	-30% in 2.4mg group, -15% in 1.2mg group, -9% in 0.6mg group, vs. -6% in placebo	-34% in 1.8mg group, -20% in 1.2mg group, vs. +3% in placebo	
	HDL	+15% in 2.4mg, +12% in 1.2mg, +8% in 0.6mg vs. +2% in placebo	+27% in 1.8mg group, -24% in 1.2mg group, vs. -1% in placebo	
	TG	-20% in 2.4mg group, -9% in 1.2mg group, -9% in 0.6mg group, vs. -8% in placebo	-19% in 1.8mg group, -1.3% in 1.2mg group, vs. +0.6% in placebo	
	Other major efficacy findings	Improvement on hunger, satiety, fullness and prospective food intake; improvement on adiponectin, leption, and CRP levels	Improvement on adiponectin, leption, and CRP levels	
Safety Results	Sleep disturbance	28.6% in 2.4mg, 18.9% in 1.2mg, 5.4% in 0.6mg vs. +15.8% in placebo	16.7% in 1.8mg for nightmare	
	Insomnia	48.6% in 2.4mg, 29.7% in 1.2mg, 21.6% in 0.6mg vs. 21.1% in placebo	16.7% in 1.8mg only	
	Diarrhea	31.4% in 2.4mg, 13.5% in 1.2mg, 13.5% in 0.6mg vs. 15.8% in placebo	/	
	Nausea	45.7% in 2.4mg, 29.7% in 1.2mg, 21.6% in 0.6mg vs. 26.3% in placebo	/	
	Vomiting	22.9% in 2.4mg, 2.7% in 1.2mg, 8.1% in 0.6mg vs. 10.5% in placebo	/	
	Overall safety	Sleep disturbance and gastrointestinal AE were more common with beloranib than placebo; generally mild to moderate and transient; High withdrawal rate in 2.4mg arm: 17/35 or 48.6%, primarily due to sleep disturbance reflective of increased sleep latency	Both 1.2mg and 1.8mg Beloranib appeared to be well-tolerated. The rate and severity of treatment-emergent AEs was comparable among the three treatment groups. There were no deaths, SAEs, or severe AEs reported in this clinical trial as related to any treatment.	

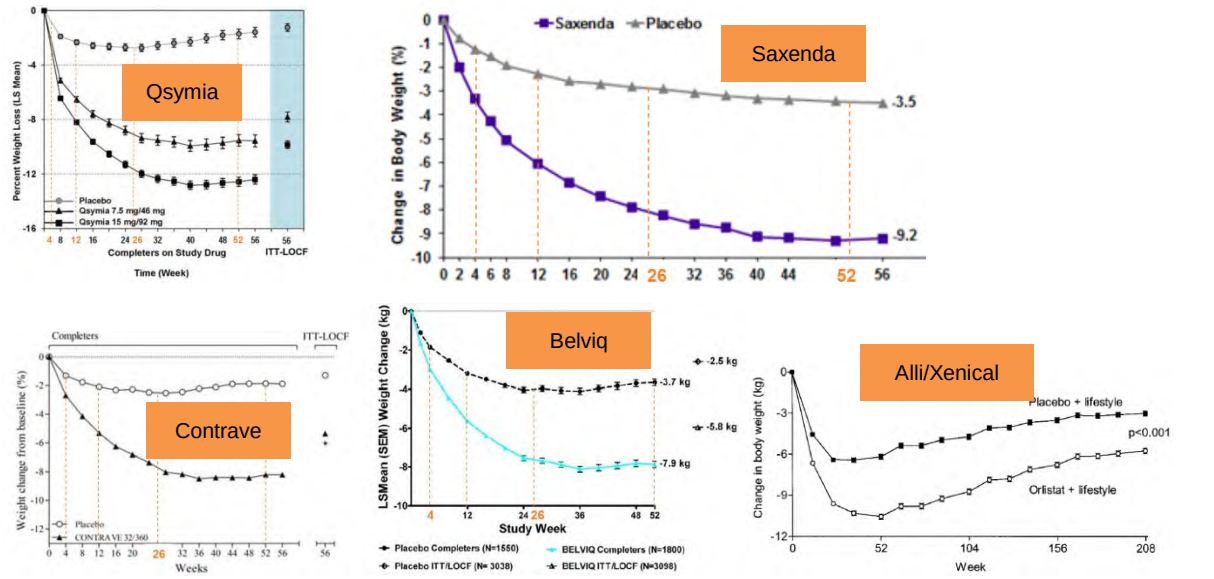
Note: important information is highlighted in red; Source: ClinicalTrials.gov, Zafgen reported data, SunTrust Robinson Humphrey

<u>Is beloranib's efficacy durable during a six-month period?</u>

We believe the efficacy of beloranib should last beyond four to 12 weeks. We expect that weight reduction may not plateau before week 26 or even before week 40 according to an analysis of previously approved obesity drugs.

We compare the weight reduction effect for obesity drugs currently on the U.S. market approved for long-term use, namely Qsymia, Belviq, Contrave, Saxenda, and Xenical/Ali. These drugs employ distinct mechanisms of action working through the central nervous system, peripheral endocrine system, or GI system. All of them demonstrate persistent weight reduction and the effect plateaus between 32 weeks (Contrave) and 40 weeks (Qsymia and Saxenda).

Exhibit 35: Pivotal Trial Data for Qsymia, Saxenda, Contrave, Belviq, and Alli/Xenical



Source: Prescribing Information from FDA.gov, SunTrust Robinson Humphrey

With regard to the relative weight reduction at week 4 or week 12 as compared to week 26, these drugs demonstrate an average Wk4/Wk26 ratio of 32% and Wk12/Wk26 ratio of 67%. Beloranib demonstrated a weight reduction of ~2.5kg at week 4 among completed trials at the ~1.8mg dose, and 10.5kg at week 12 in the ZAF-201 Phase IIa trials. Therefore, we project that a placebo-adjusted weight reduction of 7.9kg to 15.7kg could be attainable for beloranib at week 26 in the ongoing Phase III trial for PWS.

Exhibit 36: Placebo-Adjusted Weight Reduction Comparison and Projection

	Qsymia (7.5mg/46mg)	Belviq	Contrave	Saxenda	Average	Beloranib
Week-4	2.5%	1.0kg	1.5%	2.0%	/	~2.5kg on average
Week-12	4.5%	2.5kg	3.5%	3.8%	/	~10.5kg @2.4mg
Week-26	7.0%	3.5kg	5.5%	5.0%	/	**7.9kg to 15.7kg projected**
Week-52	8.0%	4.2kg	6.5%	5.7%	/	
Wk4/Wk26	31.3%	28.6%	27.3%	40.0%	**31.8%**	
Wk12/Wk26	56.3%	71.4%	63.6%	76.0%	**66.8%**	

Source: SunTrust Robinson Humphrey

Is 2.4mg beloranib tolerable?

In the ZAF-311 Phase III trial for beloranib in treating PWS, a higher dose of 2.4mg will be studied to replace the 1.2mg dose used in the ZAF-211 Phase IIa trial for PWS. In the ZAF-201 trial for beloranib in treating severe obesity patients however, 2.4mg and 3.2mg beloranib were not well tolerated and resulted in a high withdrawal rate, primarily due to sleep disturbances or other sleep related issues.

We believe sleep related tolerability issues should not be a major problem in the 2.4mg beloranib arm in the Phase III trial for PWS. Sleep disturbances and sleep latency were not observed in the ZAF-211 Phase IIa trial for beloranib in PWS or ZAF-221 Phase IIa trial for beloranib in HIAO. Major sleep related issues observed in the ZAF-211 or ZAF-221 trials were one case (16.7%) of nightmare and one case (16.7%) of insomnia in the ZAF-211 trial. The better tolerability for sleep related issues observed in trials with PWS or HIAO patients are likely due to hyper-somnolence or hypersomnia commonly observed in PWS or HIAO patients. Excessive daytime sleepiness is a common symptom in PWS patients, which may be attributable to primary hypothalamic dysfunction. We believe this high baseline level of somnolence could potentially neutralize sleep disturbances associated with beloranib treatment. Our KOL consultants do not believe sleep disturbances are a major tolerability issue for PWS or HIAO patients.

As the 1.8mg dose was less efficacious than the 1.2mg dose, will the 2.4mg dose be even less efficacious?

In the ZAF-211 Phase IIa trial 1.2mg appears to demonstrate better weight reduction than 1.8mg. However, as discussed previously, management noted that the reason for a high standard error and a lack of dose-dependent reduction observed in the weight reduction results were primarily due to patient compliance issues, which would be addressed in the ongoing Phase III trials. One method is to limit the time PWS patients stay at group homes to less than 50%.

Body fat composition assessed by DEXA scan, which we believe is a more objective measurement with less human interference, does show a dose dependent response in reducing fat mass (refer to Exhibit 28 on page 31).

Does the use of co-primary endpoints increase or decrease the bar for approval? How impactful is the change?

The co-primary endpoints represent a higher bar to achieve as compared to a single primary endpoint since theoretically the trial has to meet both clinical endpoints with statistical significance in order to be successful. We believe the co-primary endpoints could be achievable based on promising data from previous trials and the power assumptions of the ZAF-311 trial (90% powered to demonstrate a 1.5% reduction of body weight and 4.5 units reduction in the PWS questionnaire). Additionally, the FDA lowered the bar of the required statistical significance to p <0.05 from p <0.025. A higher required p value indicates an increased margin of error being tolerated for the ongoing Phase III trial, suggesting a less stringent requirement.

The ZAF-211 Phase IIa trial only reported the effect of beloranib in reducing body weight, and PWS-HQ score individually. Statistically, in order to assess the probability that beloranib has effects on both endpoints, we need to understand the covariance or correlation between the two endpoints. For example, on one end of the spectrum if both endpoints have perfect positive correlation (correlation=1), achieving either endpoint is equivalent to passing both endpoints. On the other end of the spectrum, if both endpoints have perfect negative correlation (correlation=-1), an increase of one variable indicates a decrease in the other variable. Zafgen hasn't provided any specific analysis with regard to the correlation of these two endpoints from the ZAF-211 trial and the number of patients might be too small to be conclusive. However, the Company noted that they were "fairly comfortable" that PWS-HQ was reflective of the underlying drive to hunger in PWS patients and was well-correlated with weight loss, as both were "reflective of the drug's intrinsic effects." Our conversations with pediatric endocrinologists suggest that weight gain (or obesity) and hyperphagia behavior are likely closely correlated, echoing the aforementioned comment from Zafgen.

Even if only one of the clinical endpoints is met with statistical significance, our expert consultants suggest that the drug could still have a clinically meaningful benefit for PWS patients. In this case, management commented that they would still move forward with a regulatory submission. We believe the FDA could look at the totality of the data to determine the approvability of beloranib for the treatment of PWS, which has a significant unmet medical need.

Is the trial sufficiently powered?

The ZAF-211 Phase IIa trial for PWS and ZAF-221 Phase IIa trial for HIAO were proof-of-concept trials and were not powered to demonstrate efficacy with statistical significance. The ZAF-311 trial, according to management, was 90% powered to demonstrate a 1.5% difference in weight reduction between treatment groups and placebo at the end of six months. As discussed previously, we believe 1.5% is a low bar to beat as four week results in the completed trials for beloranib already demonstrated a weight reduction of over 1.5%.

With regard to the PWS-HQ total score, the questionnaire used in the Phase IIa trial included 10 questions with a scale of 0 to 40. And in the ongoing Phase III trial, the total score is between 0 and

36 with one question removed by request of the FDA. The Phase III trial is powered to demonstrate a 4.5-unit difference between treatment groups and placebo. Baseline scores were 8.2, 7.5, and 12.5 as demonstrated in the exhibit below, and changes of +40%, +5%, and -50% were observed after four weeks of treatment in the placebo, 1.2mg beloranib, and 1.8mg beloranib arms, respectively.

Exhibit 37: Baseline Patient Characteristics in the ZAF-211 Trial

		Beloranib	
Characteristic (mean (SD) or number (%))	**Placebo (N=6)**	**1.2mg (N=5)**	**1.8mg (N=6)**
Female, n (%)	3 (50.0)	4 (80.0)	4 (66.7)
Age, years	32.5 (4.8)	37.2 (10.8)	31.5 (9.8)
Weight, kg	69.9 (16.7)	66.4 (9.6)	78.2 (15.3)
BMI, kg/m^2	29.8 (5.3)	29.4 (3.4)	34.7 (5.8)
Confirmed diagnosis of PWS			
Uniparental disomy	3 (50.0)	1 (20.0)	2 (33.3)
Chromosome 15 microdeletion	3 (50.0)	4 (80.0)	4 (66.7)
Hyperphagia Questionnaire Total Score	8.2 (9.2)	7.5 (6.1)	12.5 (5.8)
Pre-study daily caloric allowance	1142 (388)	1130 (254)	917 (98)
Adiponectin, mg/mL	6.2 (4.4)	6.6 (2.5)	4.8 (1.8)
hsCRP (mcg/mL)	2.5 (1.9)	3.1 (3.8)	1.4 (0.9)
Leptin, ng/mL	16.1 (5.1)	27.6 (11.3)	32.0 (13.5)
HDL cholesterol, mmol/L	1.1 (0.3)	1.4 (0.3)	1.1 (0.2)
LDL cholesterol, mmol/L	2.3 (0.8)	2.1 (0.7)	2.5 (0.9)
Total cholesterol, mmol/L	3.8 (0.8)	4.1 (0.5)	4.0 (1.1)
Triglycerides, mmol/L	2.4 (1.2)	1.9 (0.7)	2.0 (0.7)
Total body mass, kg	69.7 (15.3)	65.5 (9.6)	77.7 (15.5)
Total body fat mass (DEXA), kg	31.1 (9.2)	29.5 (7.2)	39.0 (9.9)
Total body lean mass (DEXA), kg	36.2 (7.8)	34.1 (2.9)	36.3 (7.9)

Source: Zafgen reported data, SunTrust Robinson Humphrey

Therefore the changes of PWS-HQ total score from baseline were +3.3, +0.4, and -6.2 respectively. Placebo adjusted difference were -2.9 units in the 1.2mg beloranib arm, and -9.5mg in the 1.8mg beloranib arm. We believe a 4.5-unit change should be attainable in the Phase III PWS trial with the higher doses of 1.8mg and 2.4mg beloranib.

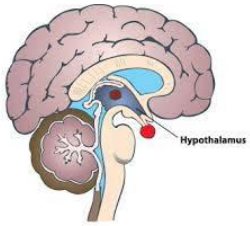
HIAO: Hypothalamic Injury Associated Obesity

HIAO is a Second Rare Obesity Target for Beloranib

HIAO is caused by damage to the hypothalamus, which most commonly occurs during surgical removal of a craniopharyngioma, a central nervous system tumor. Other diseases or treatment, including stroke, brain trauma or radiation for cancer patients may also lead to HIAO, but they are less frequently observed among HIAO patients and only account for 10% of all HIAO cases.

The hypothalamus is an area in the brain that is located below the thalamus and above the pituitary gland and brain stem with the size being close to that of an almond.

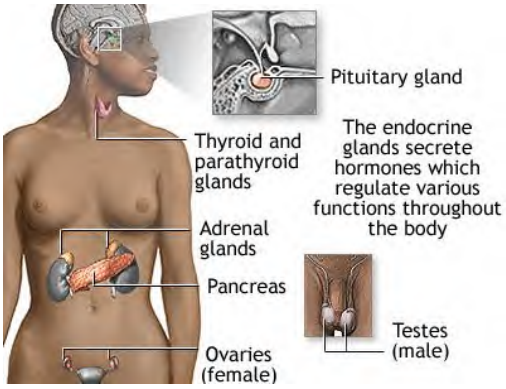
Exhibit 38: The Hypothalamus



Source: SunTrust Robinson Humphrey

The hypothalamus is a link between the nervous system and the endocrine system via the pituitary gland. It plays an important role in regulating the endocrine system and controlling important biological functions including heart rate, blood pressure, body temperature, hunger, body weight, sleep cycles, and hormone production by the pituitary gland. When the hypothalamus is damaged, hyperphagia develops and intractable weight gain ensues.

Exhibit 39: Human Endocrine System



Source: National Institutes of Health

A craniopharyngioma is a non-cancerous tumor that develops in the brain close to the pituitary gland, which most commonly affects children five to 10 years of age. Approximately 30% to 50% of craniopharyngioma cases are diagnosed at childhood and adolescence. Craniopharyngioma causes a series of symptoms due to its impact to the brain:

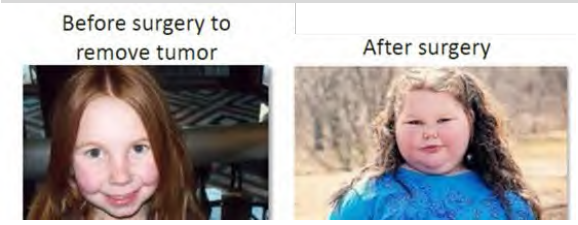
- Headache, nausea, vomiting, and difficulty with balance caused by increased pressure on the brain
- Excessive thirst, excessive urination, and stunted growth due to damage to the pituitary gland and hormone imbalances
- Decreased vision due to pressure or damage to the optic nerve

In the U.S., it is estimated that approximately 350 new cases of craniopharyngioma are diagnosed each year, or approximately 0.1 per 100,000 per year. Orphanet estimates that the point prevalence of craniopharyngioma is approximately 1:50,000. Other published population studies estimate that the incidence of craniopharyngioma is between 0.13 to 0.17 per 100,000 per year in the U.S. and EU. Craniopharyngioma constitutes approximately 1% to 3% of all brain tumors and approximately 5% to 10% of brain tumors in children.

Surgery is indicated in almost all craniopharyngioma cases, with the goal of alleviating mass-related symptoms by removing as much tumor as safely possible. A high frequency of hypothalamic obesity, between 30% and 77%, has been reported following craniopharyngioma treatment. In a report of 42 adults with tumors in the hypothalamic region (treated with surgery and/or radiotherapy), 52% of patients were obese after a median of five years of follow-up (versus 24% at baseline).

Depending on the level of damage to the hypothalamus caused by tumor removal and radiation, there may be varying degrees of hyperphagia and obesity. Our consultants noted that severe obesity with a BMI over 40kg/m^2 is not uncommon among HIAO patients.

Exhibit 40: HIAO Patient Before and After Surgery



Source: Zafgen public presentation

There is a significant unmet medical need for HIAO patients as no drug has been approved to date by the FDA. Our consultants noted that hyperphagia in HIAO patients could be severe and very difficult to manage. Obesity is therefore very likely to ensue for these patients. Our expert cited one patient that had a craniopharyngioma removed during adulthood. The patient, an athletic female with a body weight of 120 pounds before surgery and had several children, gained 50 pounds within one year after surgery. Our physician expert commented that hyperphagia and weight gain was very difficult to manage for adult HIAO patients, let alone for children.

Current management for HIAO patients includes lifestyle management. However, due to a slower metabolism and consistent hunger, lifestyle change could be challenging and its effect not satisfactory. Bariatric surgery could work for HIAO patients, but it is currently employed in less than 5% of HIAO patients, according to our consultants, due to resistance to additional surgery and concerns over side effects from patients and family.

As the hypothalamus is not amenable to therapy, theoretically pharmacotherapy needs to address alternative pathways to control hyperphagia and obesity. Serotonin or norepinephrine reuptake inhibitors, including phentermine, fenfluramine, fluoxetine, sibutramine, etc., have demonstrated minimal efficacy. One study demonstrated that sibutramine (withdrawn from the market) had a small but reproducible effect in BMI. It is believed that these medications work centrally to reduce food

intake, but do not work peripherally to stimulate skeletal muscle to increase energy expenditure or decrease biosynthesis of fat. Therefore, they may have limited efficacy in HIAO or PWS patients which have impairment of the hypothalamus.

Our model assumes a 2020 approval for beloranib in the treatment of HIAO. We estimate total WW revenue booked by Zafgen for beloranib of approximately $260 million for this indication in the out year of our model, 2025.

Phase IIa Results in HIAO are Promising

ZAF-221 Phase IIa Trial

In January 2015 Zafgen announced that ZAF-221 had met the primary efficacy endpoint of weight reduction (p=0.01) in a Phase IIa trial for beloranib in treating patients with HIAO. Beloranib treatment was well-tolerated. The randomized, double-blind trial with 14 HIAO patients at four trial sites (two in the U.S. and two in Australia) compared 1.8mg beloranib to placebo for four weeks with an optional four-week open-label extension period. Initiated in June 2014, this trial completed enrollment in September 2014, top-line data was released in January 2015, and the Company presented the results in a poster presentation at the Endocrine Society Annual meeting (ENDO) in March 2015.

The primary outcome measure was change in body weight from baseline to week-four; and secondary outcome measures included change from baseline to week-four for: lipid profile (cholesterol, LDL, HDL, triglycerides), high sensitivity C-reactive Protein (hs-CRP), and hunger and appetite using an eight-question Visual Analog Scale (Flint 8Q-VAS).

Key inclusion and exclusion criteria were:

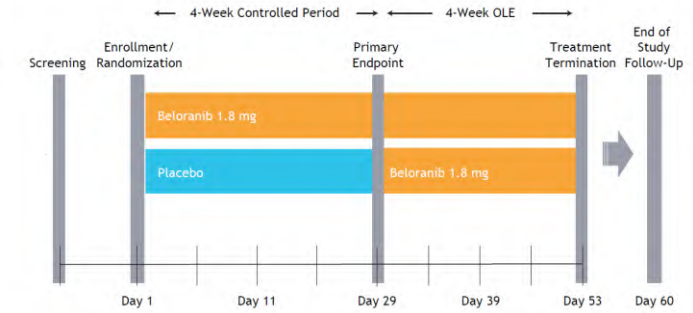
Major Inclusion Criteria

- 18 to 65 years of age
- Obesity as a consequence of acquired anatomical hypothalamic damage with BMI ≥30kg/m^2 and ≤60kg/m^2
- ≥ six months post-treatment, including chemotherapy, surgery or radiation with resulting injury to the hypothalamus and/or the pituitary
- Stable body weight for ≥ three months
- Type 2 diabetes mellitus allowed if HbA1c <10%, fasting glucose <240mg/dL

Major Exclusion Criteria

- Use of weight loss agents, including herbal medications, in the past three months
- Type 1 diabetes mellitus
- Metabolic disorders or genetic disorders linked to obesity
- History of bariatric surgery

Exhibit 41: ZAF-221 Clinical Trial Design



Source: Zafgen reported data, SunTrust Robinson Humphrey

Adult patients with magnetic resonance imaging confirmed hypothalamic injury and rapid weight gain following resection of craniopharyngioma (n=13) or pituitary macroadenoma (n=1) were randomized to one of two arms: six patients in the placebo arm and eight in the 1.8mg beloranib arm.

The average age of patients was approximately 32 years and the average BMI was 43kg/m^2. Baseline characteristics were evenly distributed between the two arms with the exception that the beloranib arm had higher total cholesterol, LDL and triglyceride levels.

Exhibit 42: Demographic and Clinical Characteristics Determined at Screening (Safety Population)

	Beloranib 1.8 mg (N=8)	Placebo (N=6)
Female, n (%)	5 (62.5)	4 (66.7)
Age, years (mean, [SD])	30.0 (9.5)	34.3 (8.8)
Body weight, kg (mean, [SD])	127.6 (22.8)	124.8 (23.0)
BMI, kg/m^2 (mean, [SD])	43.4 (8.0)	42.1 (6.0)
Etiology of injury, n (%)		
- Craniopharyngioma	8 (100)	5 (83.3)
- Pituitary macroadenoma	0	1 (16.7)
Time from confirmed hypothalamic injury, years	9.0 (10.1)	11.4 (9.4)

Source: Zafgen reported data, SunTrust Robinson Humphrey

Exhibit 43: Mean (SD) Baseline Laboratory Values (Per Protocol Population)

	Beloranib 1.8 mg (N=8)	Placebo (N=4)
Total cholesterol (mg/dL)	198.4 (40.2)	174.3 (66.0)
LDL cholesterol (mg/dL)	134.0 (37.6)	71.3 (36.6)
HDL cholesterol (mg/dL)	41.9 (5.7)	49.0 (34.7)
Triglycerides (mg/dL)	180.0 (102.3)	142.5 (23.6)
Fasting plasma glucose (mg/dL)	92.5 (22.6)	88.3 (19.4)
hsCRP (mg/L)	19.9 (11.1)	14.4 (12.3)

Source: Zafgen reported data, SunTrust Robinson Humphrey

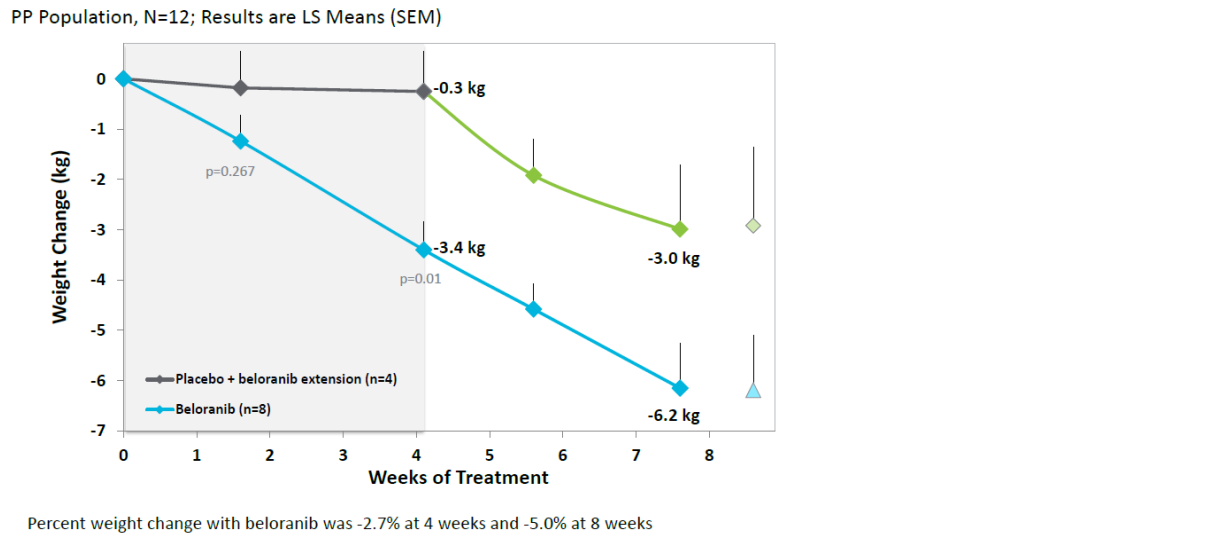
All patients in the beloranib arm completed the randomized portion of the trial, while one patient in the placebo group discontinued due to sensitivity to the placebo injection.

The trial achieved its primary endpoint of weight reduction with statistical significance of *p* =0.01 after the four-week randomization period. At the end of the beloranib open-label extension phase, the original placebo group saw a weight loss of approximately 3.0kg, and the original beloranib group saw an additional 2.8kg weight loss for a total 6.2kg weight loss as compared to the baseline weight measurement.

We believe that given the small sample size and short duration of the trial the data are very encouraging with beloranib demonstrating a clinically meaningful and consistent weight loss in various comparisons:

- At week four: beloranib vs. placebo, Δ=3.1kg
- At week eight: beloranib vs. placebo, Δ=3.2kg
- In the placebo arm: end of eight-week vs. end of week four, Δ=2.7kg
- In the beloranib arm: end of eight-week vs. end of week four, Δ=2.8kg

Exhibit 44: ZAF-221 Phase IIa Trial Results



Note: the two data points on the far right side were assessed at the end of study follow-up, which is seven days after treatment termination at day 53;
Source: Zafgen public presentation, SunTrust Robinson Humphrey

Beloranib was well-tolerated. There were no deaths or serious adverse events reported, neither were there discontinuations due to adverse events in patients treated with beloranib. Key tolerability issues included mild increase in sleep onset and mild dizziness. Mild and transient dizziness, headache, and nasopharyngitis (two patients or 25.0%) were the only TEAEs occurring in more than one patient in the beloranib arm. Headache occurred in two (33.3%) patients and nasopharyngitis occurred in one (16.7%) patient in the placebo arm.

The Company noted that no safety concerns were found from clinical laboratory results and no changes in ECG findings, BP or heart rate were observed with beloranib treatment.

Exhibit 45: Summary of TEAEs during Double-Blind Treatment (Safety Population)

	Number (%) of Patients	
	Beloranib 1.8 mg (N=8)	Placebo (N=6)
Patients with any AE	7 (87.5)	4 (66.7)
Total number of AEs	36	12
Total number of moderate intensity AE	5	2
Severe intensity AE	0	0
Serious AE	0	0
AE leading to withdrawal	0	1 (16.7)
AE leading to death	0	0

Source: Zafgen data, SunTrust Robinson Humphrey

We believe the ZAF-221 trial successfully demonstrated a rapid and significant weight loss in HIAO patients treated with beloranib. Efficacy in patients with impaired hypothalamic structures broadens the application of beloranib beyond genetic obesity disease such as PWS, and supports an extra-hypothalamic mode of action for beloranib. A benign safety profile bodes well for long-term use of beloranib. Our consultants that specialize in the treatment of HIAO praised the data demonstrated in the ZAF-221 trial and commented that it was one of the cleanest data sets they had seen. Although our expert was hesitant to assign a number with regard to the probability of success in Phase III trials for beloranib in HIAO, they noted that if the Phase III trials could reproduce what was observed in the Phase II trial, beloranib should be approvable. And they had no reason to say that the trial might fail other than it was a small trial.

For the next step, Zafgen is establishing U.S. and EU regulatory pathways for Phase III clinical trials for beloranib in treating HIAO.

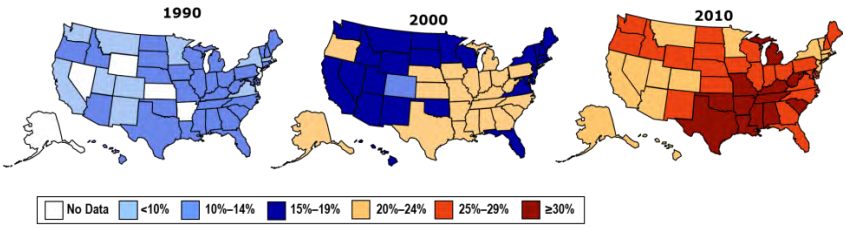
Severe Obesity

Introduction to Severe Obesity

Zafgen is developing beloranib for the treatment of severe obesity patients complicated with type 2 diabetes. Obesity is a medical condition in which excess fat accumulates in the body. Obesity occurs over time when energy intake from food is consistently more than energy expenditure from physical activities or from the maintenance of a constant body temperature. It has been shown that obesity increases the risk of diabetes, heart disease, stroke, arthritis, etc. An estimated 5% to 10% decrease of body weight could delay or prevent some of these diseases. Obesity has become a pandemic in the U.S. according to data from the NIH:

- More than two in three adults (225 million) are considered to be overweight or obese (BMI ≥25).
- More than one in three adults are considered to be obese (BMI ≥30).
- More than one in twenty adults are considered to have severe obesity (BMI ≥40).
- Approximately one-third of children and adolescents ages 6 to 19 are considered to be overweight or obese (at or above the 85th percentile).
- More than one in six children and adolescents ages 6 to 19 are considered to be obese (at or above the 95th percentile).

Exhibit 46: Obesity[1] Trends among U.S. Adults



Note: [1]BMI ≥ 30; Source: Centers for Disease Control (CDC), SunTrust Robinson Humphrey

Body mass index (BMI) is the tool most commonly used to measure obesity in children and adults and is defined as weight in kilograms divided by height in meters squared. Children grow at different rates at different times, so it is not always easy to determine if a child is obese. BMI charts for children compare their height and weight to other children of the same sex and age.Severe obesity is defined as a BMI ≥40 kg/m^2 (or ≥35 kg/m^2 in the presence of co-morbidities).

The treatment of obesity includes lifestyle programs, e.g., behavior modification, diet, exercise; drug therapy; and bariatric surgery. Many obesity drugs had been approved but most were withdrawn primarily due to safety concerns. Several obesity pharmacotherapies have been approved by the FDA since 2012, namely Qsymia, Belviq, Contrave, and Saxenda.

Exhibit 47: Anti-Obesity Drugs – Approved, In-Development, and Withdrawn

Drug	Mechanism of Action	Target System	Weight Reduction	Introduced-Withdrawn, or Clinical Stage	Comment
Approved in U.S. or EU					
Phentermine	Noradrenaline releaser, sympathomimetic	CNS	Variable	1959–present (only in US)	Only for short-term use in patients without hypertension
Alli/Xenical (orlistat)	Gastric and pancreatic lipase inhibitor	GI	3%	1999–present	Fatty and oily stools are the major side effects
Belviq (lorcaserin)	5HT2C receptor agonist	CNS	3.1-3.3%	2012–present (only in US)	Moderate efficacy with side effects like dizziness, headache, insomnia
Qsymia (phentermine and topiramate)	Noradrenaline releaser and anti-convulsant	CNS	6.6%-9.4%	2012–present (only in US)	Side effects include dizziness, headache, insomnia
Contrave (naltrexone and bupropion)	Opioid receptor antagonist/noradrenaline/dopamine reuptake inhibitor	CNS	2.0-4.1%	2014-present (only in US)	Cardiovascular side effects
Saxenda (liraglutide)	GLP-1 receptor agonist	GI	3.7-4.5%	2014-present (only in US)	Not be used in patients with a history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2 (black box warning); not be taken during pregnancy
In Clinical Development					
Empatic (bupropion with zonisamide)	Noradrenaline/dopamine reuptake inhibitor and anti-convulsant	CNS	8.2%	Phase IIb completed	Side effects include nausea, headache, insomnia, anxiety
Tesofensine	Serotonin/noradrenaline/dopamine reuptake inhibitor	CNS	/	Phase II completed	Depressed mood, possibly cardiovascular side effects, increased blood pressure and heart rate
Oblean (cetilistat)	Pancreatic lipase inhibitor	GI	1.7%	Approved in JPN (2013-present)	Side effect profile similar to orlistat
Beloranib	**MetAP2 inhibitor**	**CNS+liver+ adipocytes**	**/**	**Phase III for PWS Phase IIb for severe obesity**	**No serious side effects reported; sleep and GI side effects are more frequent**
Velneperit	Neuropeptide Y5 receptor antagonist	CNS	/	Phase II	No psychiatric side effects reported
rm-493	Selective peptide agonist for the melanocortin 4 receptor	CNS	/	Phase II for PWS Phase II for obesity	
Pramlintide	Analog of amylin	GI	/	Phase II - likely suspended	
TT-401 (LY2944876)	Glucagon/GLP-1 dual agonist	GI	/	Phase II	Decreased appetite with mild nausea and vomiting
PP1420	Pancreatic polypeptide analog	GI	/	Phase I	No serious adverse effects reported
GSK598809	D3 (dopamine) antagonist	CNS	/	Phase I completed	Headache, somnolence, feeling drunk, dizziness, fatigue, pain at infusion site, nausea and vomiting
ZP-2929	Glucagon/GLP-1 dual agonist	GI	/	Phase I	No serious adverse effects reported
Withdrawn from Market					
Fen-Phen (fenfluramine/ phentermine)	Serotonin/noradrenalin releasers	CNS	/	1992–1997 (only in US)	Valvular heart disease, pulmonary hypertension
Rimonabant	CB1 receptor antagonist	CNS	/	2006–2008 (only in EU)	Side effects include depression and anxiety
Sibutramine	Serotonin/noradrenalin reuptake inhibitor	CNS	/	1997–2010	Increased risk for stroke and myocardial infarction
2,4-Dinitrophenol (DNP)	Uncoupling oxidative phosphorylation in mitochondria	Ubiquitous	/	1933–late 1930s	Increased body temperature, nausea, vomiting, sweating, dizziness, headache and death
Amphetamine	Increasing synaptic dopamine, norepinephrine and serotonin	CNS	/	1930–late 1970s	Side effects include disturbances of mood and behavior, cardiac and gastrointestinal effects

Note: CNS: central nervous system, GI: gastrointestinal, Source: SunTrust Robinson Humphrey, Diabetes Metab Syndr Obes. 2014; 7: 73–84;Trends Neurosci. 2013 Feb;36(2):133-40.; Zafgen public filings

The most effective treatment for severe obesity is bariatric surgery, including Roux-en-Y gastric bypass, adjustable gastric banding, sleeve gastrectomy, and bilio-pancreatic diversion. Bariatric surgery could be indicated for patients with a BMI ≥40kg/m^2 who have failed to lose weight with diet, exercise, and drug therapy; or individuals with a BMI >35kg/m^2 with obesity-related comorbidities (e.g., hypertension, impaired glucose tolerance, diabetes mellitus, dyslipidemia, sleep apnea) who have failed diet, exercise, and drug therapy.

Bariatric surgery produces rapid and profound weight loss with an average from 50% to 70% two years post-procedure, but can result in adverse events including thrombotic events, infection, internal bleeding, pulmonary disease, etc. Bariatric surgery is not indicated for glycemic or lipid control, or for cardiovascular risk reduction independent of the BMI parameters. It is contraindicated for patients with psychiatric conditions such as major depression or psychosis, binge-eating disorders, drug and alcohol abuse, etc. Bariatric surgery in the elderly (>65 years of age) or

adolescent patients (<18 years of age) is controversial, but may be considered if co-morbidities are severe.

Despite Approval of New Drugs an Unmet Need Still Exists

The pharmaceutical industry has made significant efforts to develop new drugs for the treatment of obesity. Four of the six obesity drugs on the U.S. market have been approved by the FDA since 2012. Despite this advancement, existing obesity drugs have undesirable tolerability and safety profiles.

Exhibit 48: Approved Obesity Drugs in the U.S.

Drug	% Placebo-Adjusted Weight Loss*	Key Limitations
Phentermine	Variable	• Short-term (a few weeks) use only • Not be taken during pregnancy
Xenical/alli	3%	• Unpleasant gastrointestinal side effects related to dietary fat malabsorption • Not be taken during pregnancy
Qsymia	6.6%-9.4%	• Human teratogen – not be used in women unless contraception can be assured
Belviq	3.1%-3.3%	• Not be taken during pregnancy or by women who are planning to become pregnant
Contrave	2.0%-4.1%	• Patients should be monitored for suicidal thoughts and behaviors (black box warning, antidepressant class labeling) • Not be taken during pregnancy
Saxenda	3.7%-4.5%	• Not be used in patients with a history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2 (black box warning) • Not be taken during pregnancy

Source: Zafgen public filings, drug prescribing information, SunTrust Robinson Humphrey

We believe beloranib has demonstrated a rapid and significant weight reduction with an ~10% placebo adjusted weight loss in 12 weeks, and a relatively benign safety profile. The favorable efficacy and safety profile could be meaningful for patients with severe and complicated obesity.

Clinical Development

Zafgen originally developed beloranib to treat obesity including severely obese patients with BMIs up to 60kg/m^2. The first three clinical trials, ZAF-001 Phase Ib, ZAF-003 Phase Ib and ZAF-101 Phase Ib, were studied in a total of 81 obese female patients with different doses and routes of administration. The Company established a working dose range for beloranib that is between 0.65mg and 3mg. Initially Zafgen didn't have animal safety covering males and they lacked information on embryo-fetal development, so the Company initiated the work in females without reproductive potential. Later, Zafgen discovered a fully reversible impact for beloranib on spermatogenesis in animals which occurred with a window that supported male dosing in clinical trials. The Company has assessed testicular function in male subjects in the ZAF-201 trial and found no issues.

Subsequently, Zafgen conducted the Phase IIa ZAF-201 clinical trial that administered beloranib (0.6mg, 1.2mg, and 2.4mg) or placebo via SubQ injection BIW in 124 obese patients for 12 weeks. Among all the clinical trials completed by Zafgen, the ZAF-201 trial had the longest treatment

duration at 12 weeks, as compared to four weeks in other trials. The trial demonstrated that beloranib's efficacy continued beyond four weeks.

Zafgen is conducting a Phase IIb ZAF-203 clinical trial for beloranib in treating severe obesity in the general obese population with type 2 diabetes. The Company expects to enroll approximately 150 patients for a period of 12 months with interim six-month data anticipated in 4Q15 or 1Q16. A summary of all trials conducted by Zafgen relating to severe obesity are highlighted in the following exhibit.

Exhibit 49: Summary of Zafgen Clinical Trials for Severe Obesity

Trial Name	Phase	Indication	Trial type	Dosing Regimen	Treatment	Pts Number	BMI (kg/m^2)
Completed Trials							
ZAF-001	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• Escalating doses of 0.1mg/m^2, 0.3mg/m^2, and 0.9mg/m^2, or ~0.2mg, 0.6mg, and 2mg • IV BIW	4 weeks	31 (all female)	32-45
ZAF-003	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• 3.0mg, 6.0mg, and 2.5mg • 3.0mg and 6.0mg given IV BIW for 4 weeks • 2.5mg given IV BIW for the 1st week and QW for the subsequent 6 weeks	4 weeks or 7 weeks	25 (all female)	30-50
ZAF-101	Ib	Severe Obesity	Randomized, DB, Placebo-controlled	• 1.0mg, 2.0mg, and 4.0mg • SubQ BIW	4 weeks	25 (all female)	30-45
ZAF-201	IIa	Severe Obesity	Randomized, DB, Placebo-controlled	• 0.3mg, 0.6mg, 1.2mg, 2.4mg, and 3.2mg • SubQ BIW	12 weeks	160 (157 female)	30-50
ZAF-211	IIa	PWS	Randomized, DB, Placebo-controlled	• 1.2mg and 1.8mg • SubQ BIW	4 weeks	17	26-44
ZAF-221	II	HIAO	Randomized, DB, Placebo-controlled	• 1.8mg • SubQ BIW	4 weeks + 4 weeks extension	14	30-55
Ongoing Trials							
ZAF-203	IIb	Severe Obesity with T2D	Randomized, DB, Placebo-controlled	1.2mg and 1.8mg SubQ BIW	12 months with 6 months interim	150	30-60
ZAF-311 (bestPWS)	III	PWS	Randomized, DB, Placebo-controlled	1.8mg, 2.4mg SubQ BIW	6 months + 6 months open label	102+	Age 12-17: BMI≥ 95th percentile for age and gender, Age 18+: BMI 27-60

Note: highlighted trials are related to severe obesity;
Source: Zafgen public filings, SunTrust Robinson Humphrey

ZAF-001 Phase Ib Trial

ZAF-001 was a double-blind, placebo controlled, dose escalation, multiple dose trial conducted in Australia. A total of 31 Caucasian female patients, with an average age of 52.2 years and a BMI range of 32kg/m^2 to 45kg/m^2, were enrolled and treated for four weeks. Patients received 0.10mg/m^2, 0.30mg/m^2, or 0.90mg/m^2 of beloranib or placebo via intravenous (IV) infusion BIW during the duration of treatment.

According to the Company, the primary objectives of the clinical trial were to evaluate the safety and tolerability of beloranib in obese patients and to determine plasma PK/PD. A secondary objective was to determine the effect of beloranib on weight loss in obese patients. A total of 26 patients of 31 enrolled patients completed the trial as planned receiving all eight infusions. Zafgen noted that three placebo patients and two beloranib treated patients withdrew from the clinical trial due to loss of venous access or other reasons unrelated to beloranib.

The efficacy results in the per protocol population are summarized in the following exhibit:

Exhibit 50: ZAF-001 Phase Ib Trial Results

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)
Placebo	6	96	-1.2
Beloranib 0.1mg/m^2 or ~0.2mg	6	105.3	-0.9
Beloranib 0.3mg/m^2 or ~0.6mg	6	100.3	-1.3
Beloranib 0.9mg/m^2 or ~2mg	8	104.2	-3.6

Source: Zafgen public filings, SunTrust Robinson Humphrey

No drug-related SAEs were observed in the study. Headaches and gastrointestinal symptoms were the most common TEAEs across all groups including placebo and were transient and mild. Contusions or bruising at infusion sites were reported, which may have been due to difficulty in gaining IV access. There were no clinically significant changes in hematology, serum chemistry or urinalysis values in the trial. According to Zafgen, weight loss was not subjected to statistical analysis as it was a secondary clinical endpoint.

ZAF-003 Phase Ib Trial

Similar to ZAF-001, ZAF-003 was a double-blind, placebo controlled, dose escalation and multiple dose trial conducted in Australia. A total of 25 obese female patients, with an average age between 44.0 and 51.3 years and BMI range of 30kg/m^2 to 50kg/m^2, were enrolled and treated for four weeks. Three doses of beloranib, 3.0mg, 6.0mg, and 2.5mg, were studied with different schedules. 3.0mg and 6.0mg doses were given BID in a four-week period, and the 2.5mg dose was given BID for the first week and QW for in the subsequent six-week period for total of seven weeks of treatment.

Of the enrolled 25 patients, 22 completed the trial and three patients withdrew with two from the 6.0mg beloranib arm due to tolerability limitations, and one from the 2.5mg beloranib arm due to an AE deemed not to be related to beloranib.

The efficacy results in the per protocol population are summarized in the following exhibit:

Exhibit 51: ZAF-003 Phase Ib Trial Results

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)
Placebo	8	104.6	-0.1
Beloranib 3.0mg	6	102.3	-4.7
Beloranib 6.0mg	3	105.5	-6.7
Beloranib 2.5mg	5	94	-2.7

Note: statistical analysis was not performed in this proof of concept trial;
Source: Zafgen public filings, SunTrust Robinson Humphrey

The trial identified the maximum tolerated dose (MTD) of 3.0mg of beloranib administered intravenously. Weight loss was established in all doses of beloranib.

ZAF-101 Phase Ib Trial

ZAF-101 was the first trial to administer a subcutaneous (SubQ) injection of beloranib.

A total of 25 Caucasian female patients, with an average age of 46.0 to 49.9 years and BMI range of 30kg/m^2 to 45kg/m^2, were enrolled. Patients received 1.0mg, 2.0mg, and 4.0mg of beloranib or placebo via SubQ BIW during a four-week treatment period.

The efficacy results in the per protocol population are summarized in the following exhibit:

Exhibit 52: ZAF-101Phase Ib Trial Results

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

Source: Zafgen public filings, SunTrust Robinson Humphrey

No deaths or SAEs were reported in the clinical trial. There were no significant changes in laboratory parameters, electrocardiograms, or vital signs in the trial. Mild transient injection site reactions were observed in all arms and were the most common side effect.

The high dose arm of 4.0mg beloranib was not well-tolerated systemically and led to more moderate TEAEs and trial withdrawals, primarily due to gastrointestinal events and sleep disturbances.

Exhibit 53: Adverse Events in ZAF-101 Phase Ib Trial

	Placebo	Beloranib 1.0mg	Beloranib 2.0mg	Beloranib 4.0mg
Number of patients, ITT population	6	6	6	7
Sleep disturbance, # (%)	1 (16.7%)	5 (83.3%)	6 (100%)	6 (85.7%)
Abnormal dreams, # (%)	0	4 (66.7%)	5 (83.3%)	6 (85.7%)
Diarrhea, # (%)	3 (50%)	2 (33%)	1 (16.7%)	3 (42.9%)
Nausea, # (%)	2 (33%)	1 (16.7%)	1 (16.7%)	1 (14.3%)
Withdrawal, # (%)	0	0	1 (16.7%)	3 (42.9%)

Source: Zafgen reported data, SunTrust Robinson Humphrey

A total of four subjects, one in the 2.0mg beloranib group and three in the 4.0mg beloranib group withdrew from the trial due to sleep disturbances, suggesting that the 4.0mg dose might not be well tolerated.

ZAF-201 Phase IIa Trial

Among the clinical trials Zafgen has completed for beloranib to date, the ZAF-201 Phase IIa trial has the longest treatment duration of 12 weeks, as compared to four weeks in other trials, and the largest patient population of approximately 150 patients as compared to between 14 to 31 patients in other trials.

A total of 160 obese patients were randomized for the treatment of beloranib of 0.3mg, 0.6mg, 1.2mg, 2.4mg, or 3.2mg, or placebo for 12 weeks. A majority of patients were female (93.8%) and Caucasian (97.5%). The average age was 48.4 years and the BMI range was 30 kg/m^2 to 54kg/m^2. Baseline characteristics were evenly distributed among the different arms.

A total of 147 patients were included in the safety population, and 122 patients were included in the per protocol population. The difference in patient number was due to patient withdrawal, primarily in the beloranib treated arms, which will be discussed later in this report.

Efficacy results were based on the per protocol population, i.e., all randomized subjects who received at least two thirds of the total dose without any major protocol deviations); safety results were based on the safety population (all 147 subjects).

Exhibit 54: Subject Characteristics at Baseline (mean [SD])

	Beloranib			Placebo
	0.6mg	1.2mg	2.4mg	
Safety Population	37	37	35	38
Per Protocol Population	35	33	18	36
Age – yr	47.9 (14.2)	47.7 (12.2)	48.2 (10.4)	49.2 (10.5)
Weight – kg	101.17 (15.20)	100.99 (13.99)	100.97 (14.36)	101.67 (17.56)
Body mass index – kg/m^2	37.66 (5.60)	37.30 (4.54)	38.31 (5.89)	37.60 (4.38)
Systolic BP – mm Hg	127.0 (10.4)	128.8 (13.7)	126.3 (11.6)	129.9 (15.2)
Diastolic BP – mm Hg	77.9 (8.2)	81.4 (8.8)	78.2 (7.1)	80.1 (10.0)
Total Cholesterol – mmol/L	5.11 (1.02)	5.47 (0.97)	5.33 (1.24)	5.73 (1.09)
LDL Cholesterol – mmol/L	3.00 (0.86)	3.41 (0.88)	3.34 (1.13)	3.45 (0.85)
HDL Cholesterol - mmol/L	1.48 (0.39)	1.38 (0.32)	1.34 (0.27)	1.44 (0.35)
Triglycerides – mmol/L	1.37 (0.60)	1.52 (0.82)	1.43 (0.59)	1.79 (0.96)
Fasting glucose – mmol/L	5.57 (1.67)	5.32 (0.70)	5.69 (1.37)	5.53 (1.33)
CRP – mg/mL	5.84 (5.86)	5.35 (6.20)	6.56 (6.16)	6.73 (7.08)
b-hydroxybutyrate – mmol/L	0.08 (0.06)	0.08 (0.06)	0.09 (0.06)	0.07 (0.05)
Leptin - ng/mL	53.86 (27.44)	52.91 (28.36)	51.47 (21.88)	54.89 (27.90)
Adiponectin - mg/ml	4.61 (2.57)	3.99 (2.16)	3.69 (1.66)	4.00 (2.41)

Note: highlighted is patient number in Safety Population and Per Protocol Population;
Source: Zafgen poster presentation, SunTrust Robinson Humphrey

Clinical endpoints included safety and tolerability, weight loss, body composition measured by bio-impedance, and PK/PD assessment.

According to the protocol, the Safety Review Committee (SRC) for the trial reviewed interim safety and PK results after 36 patients completed at least two weeks of treatment, and recommended to eliminate the lowest dose group of 0.3mg and the highest dose group of 3.2mg, leaving the doses of 0.6mg, 1.2mg, 2.4mg and placebo to be studied for the remainder of the trial. The SRC concluded that weight loss for the 0.3mg dose was not clinically meaningful and the 3.2mg dose was not well-tolerated. Unlike what was observed in other trials, the most common TEAE leading to early termination at the 2.4mg and 3.2mg dose arms was sleep disturbance.

Realizing this tolerability issue of high dose (2.4mg+) beloranib in obesity patients from the ZAF-201 trial, Zafgen is using 1.8mg beloranib instead of the 2.4mg dose in the ongoing ZAF-203 Phase IIb trial. Patients randomized in the 1.8mg dose will receive four weeks of 1.2mg beloranib at the start of the trial to help mitigate potential sleep disturbances. However, sleep disturbances and abnormal dreams were observed in patients in the ZAF-101 Phase Ib trials at 1mg and 2mg doses as well, and one patient in the 2mg beloranib arm withdrew due to sleep disturbances. We believe sleep disturbances are a tolerability issue rather than a safety concern. But we do observe cases where tolerability issues negatively impact patient adoption and commercial prospects for a drug such as the case of Xenical/Alli's GI tolerability issue and so called "oily stool." We will follow closely with regard to the effects of current strategies employed by management to address the sleep related issues.

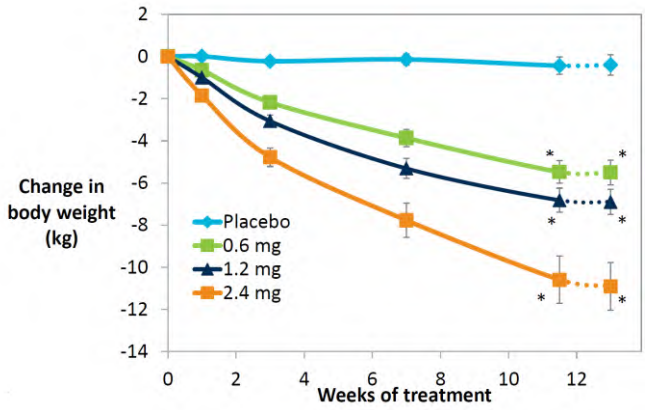
Beloranib demonstrated a statistically significant decrease in body weight in a dose-dependent manner in the per protocol population.

Exhibit 55: ZAF-201 Phase II Trial Results in Reducing Body Weight at the End of 12 Weeks

Trial Arm	Number of Patients Per Protocol	Baseline Body Weight (kg)	Average Weight Change (kg)	% Placebo-Adjusted Weight Change	*p*-value
Placebo	36	102.3	-0.4	—	—
Beloranib 0.6 mg	34	102.6	-5.5	-5	<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 public filings, SunTrust Robinson Humphrey

Exhibit 56: Body Weight Changes During the Treatment Course



*Note: Values are mean±SEM for the Per Protocol population, p values are beloranib arms vs. placebo by ANCOVA; *p<0.0001;*
Source: Zafgen reported data, SunTrust Robinson Humphrey

Cardiovascular disease risk biomarkers, including LDL, HDL, CRP, triglycerides, were measured along with other CV parameters such as blood pressure and heart rate. The results, summarized in the exhibit below, suggest that beloranib treatment did not increase the risk of cardiovascular disease and might reduce cardiovascular disease risk evidenced by a decrease in LDL and an increase in HDL.

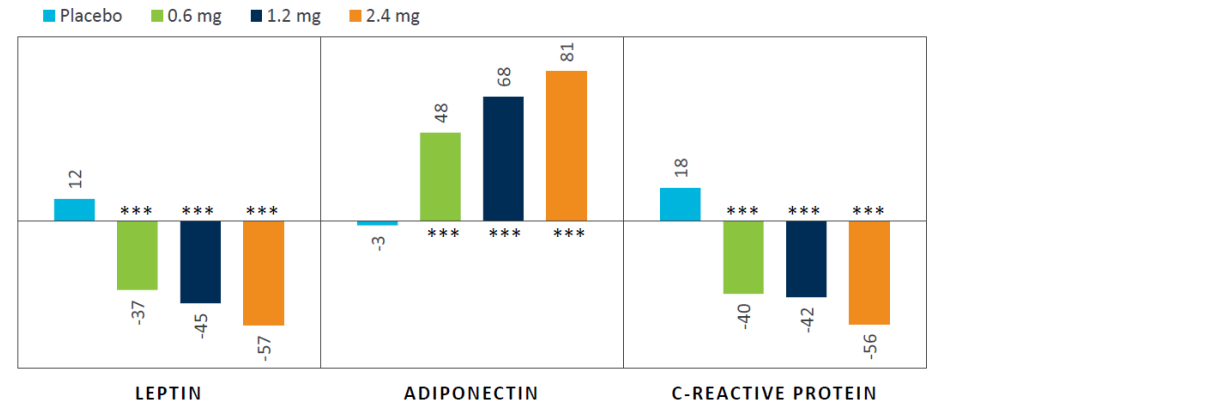
Exhibit 57: Changes from Baseline Levels of Metabolic Factors, Blood Pressure, and Heart Rate in ZAF201

Treatment Group	TG	LDL-c	HDL-c	Glucose (mmol/L)	SBP (mmHg)	DBP	Heart Rate (bpm)
Placebo							
Day 1	1.6 (0.6)	3.6 (0.8)	1.4 (0.3)	5.5 (1.3)	122 (7)	71 (8)	78 (8)
Day 81	1.5 (0.6)	3.2 (0.8)	1.4 (0.3)	5.6 (1.4)	120 (10)	70 (9)	78 (9)
% change	-8	-6	+2	+1	-1	-2	0 bpm
0.6 mg							
Day 1	1.4 (0.6)	3.0 (0.9)	1.5 (0.4)	5.6 (1.7)	125 (8)	71 (6)	79 (10)
Day 81	1.2 (0.5)	2.6 (1.0)	1.6 (0.4)	5.6 (1.1)	118 (7)	70 (8)	80 (11)
% change	-9	-9	+8	+2	-5	-3	1 bpm
1.2 mg							
Day 1	1.5 (0.8)	3.4 (0.9)	1.4 (0.3)	5.3 (0.7)	126 (9)	73 (7)	78 (8)
Day 81	1.2 (0.4)	2.8 (0.8)	1.5 (0.3)	5.4 (0.5)	120 (4)	71 (7)	78 (8)
% change	-9*	-15	+12*	+3	-5	-3	0 bpm
2.4 mg							
Day 1	1.4 (0.6)	3.3 (1.1)	1.3 (0.3)	5.7 (1.4)	128 (15)	70 (9)	81 (4)
Day 81	1.0 (0.3)	2.4 (1.1)	1.5 (0.3)	5.7 (0.7)	115 (10)	66 (7)	81 (5)
% change	-20***	-30***	+15*	+2	-12**	-6	0 bpm

*Note: TG, Triglycerides; HDL-c, High Density Lipoprotein Cholesterol; LDL-c, Low Density Lipoprotein Cholesterol; SBP/DBP, Systolic/Diastolic Blood Pressure (via 24 hr ABPM); Values are means (SD) for the Per Protocol population; p-values derived from paired t-tests for change from baseline, not corrected for repeated tests; *p<0.05, **p<0.01, ***p<0.005;*
Source: Zafgen reported data, SunTrust Robinson Humphrey

Consistent with the reduction in body weight and improvement in lipid profile, favorable changes in adiponectin, leptin and hs-CRP were observed in the beloranib arms with statistical significance at the end of the 12-week period.

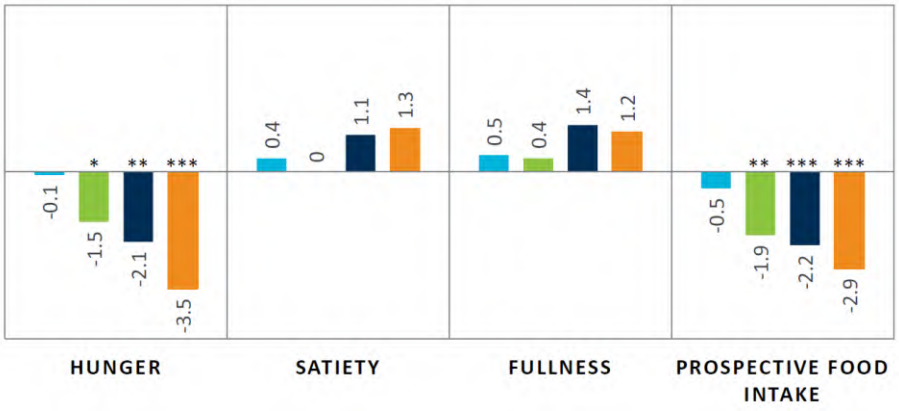
Exhibit 58: ZAF-201 Changes from Baseline Levels of Leptin, Adiponectin and CRP



*Note: ***p<0.005;*
Source: Zafgen reported data, SunTrust Robinson Humphrey

Sense of hunger, measured by a standardized eight-question visual analogue scale (8Q-VAS), was reduced by an average of 1.5, 2.2 and 3.3 as compared to an average reduction of 0.1 in placebo, respectively (p <0.05 for all doses). Baseline values were 5.0, 5.3, 5.8 and 6.4 for placebo, 0.6mg, 1.2mg and 2.4mg of beloranib, respectively.

Exhibit 59: ZAF-201 Changes from Baseline Levels of Hunger, Satiety, Fullness, and Prospective Food Intake



Source: Zafgen reported data, SunTrust Robinson Humphrey

Measurement of sense of hunger was performed with a maximum number of 10 using a standardized eight-question visual analogue scale (8Q-VAS) asking how hungry the participant had been over the prior trial period. VAS has been well studied in research, especially concerning pain and is considered the gold-standard methodology for this type of trial. 8Q-VAS in hunger was developed by Dr. Anne Flint from the Royal Veterinary and Agricultural University in 2000 and the research is widely cited and applied.

Listed below are the eight questions used in 8Q-VAS:

- **How hungry do you feel?**

I am not hungry at all……I have never been more hungry.

- **How satisfied do you feel?**

I am completely empty……I cannot eat another bite.

- **How full do you feel?**

Not at all full……Totally full.

- **How much do you think you can eat?**

Yes, very much……..No, not at all.

- **Would you like to eat something sweet?**

Yes, very much……..No, not at all.

- **Would you like to eat something salty?**

Yes, very much……No, not at all.

- **Would you like to eat something savory?**

Yes, very much……No, not at all.

- **Would you like to eat something fatty?**

Yes, very much……No, not at all.

With regard to beloranib's safety and tolerability, there were no deaths or SAEs deemed to be related to study drug. No clinically significant laboratory values or ECG/vital sign changes were observed in the trial.

The most common TEAEs were GI disorders, primarily nausea, diarrhea and vomiting; nervous system disorders, including dizziness and headache; and psychiatric disorders, such as insomnia, sleep disorder, or abnormal dreams. Laboratory assessments, vital signs and electrocardiograms revealed no unexplained abnormalities or clinically significant trends.

Sleep disturbances and gastrointestinal AEs were more common with beloranib than placebo and were generally mild to moderate and transient. Sleep related AEs appeared to have been dose related and resulted in early study withdrawal in eight subjects from the 2.4mg dose group.

Exhibit 60: ZAF-201 Adverse Events with Incidence >10%

System Organ Class / Specific AE	Placebo	Beloranib		
		0.6 mg	1.2 mg	2.4 mg
Patient number	N=38	N=37	N=37	N=35
Gastrointestinal disorders				
Diarrhea	6 (15.8)	5 (13.5)	5 (13.5)	11 (31.4)
Dry mouth	0	2 (5.4)	1 (2.7)	4 (11.4)
Nausea	10 (26.3)	8 (21.6)	11 (29.7)	16 (45.7)
Vomiting	4 (10.5)	3 (8.1)	1 (2.7)	8 (22.9)
General disorders and administrative site conditions				
Injection site pruritus	1 (2.6)	4 (10.8)	3 (8.1)	5 (14.3)
Injection site reaction	1 (2.7)	1 (2.7)	3 (8.1)	7 (20.0)
Nervous system disorders				
Dizziness	2 (5.3)	2 (5.4)	2 (5.4)	9 (25.7)
Headache	15 (39.5)	18 (48.6)	12 (32.4)	10 (28.6)
Psychiatric disorders				
Abnormal dreams	3 (7.9)	10 (27.0)	6 (16.2)	6 (17.1)
Depression	0	2 (5.4)	4 (10.8)	0
Insomnia	8 (21.1)	8 (21.6)	11 (29.7)	17 (48.6)
Sleep disorder (other)	6 (15.8)	2 (5.4)	7 (18.9)	10 (28.6)
Other				
Cough	0	1 (2.7)	2 (5.4)	4 (11.4)
Decreased appetite	7 (18.4)	11 (29.7)	12 (32.4)	9 (25.7)
Hot flush	0	4 (10.8)	2 (5.4)	8 (22.9)
Pruritis	1 (2.6)	4 (10.8)	0	0

Note: data are number (%);
Source: Zafgen reported data, SunTrust Robinson Humphrey

The high dose of 2.4mg beloranib appeared to be not as well tolerated. A total of 24 (16% of the 147 safety population) patients withdrew early from the study due to adverse events. The withdrawal rate due to adverse events was highest in the 2.4mg beloranib group (17/35 or 48.6% of the safety population). A total of nine sleep-related adverse events (mostly insomnia) led to withdrawal from the study: one in the 1.2mg beloranib arm (37 participants) and eight in the 2.4mg beloranib arm (35 participants).

A total of 21 patients treated with 2.4mg beloranib prematurely withdrew from the trial, mainly due to sleep disturbances reflective of increased sleep latency – the time patients reported taking to fall asleep at night. As discussed previously in the ongoing ZAF-203 Phase IIb trial Zafgen would employ a lower dose of 1.8mg to replace the 2.4mg used in the ZAF-201 trial, and would up-titrate patients in the 1.8mg arm with 1.2mg beloranib for four weeks to mitigate potential sleep disturbance.

ZAF-203 Phase IIb Trial

Zafgen is currently conducting a Phase IIb trial in severely obese adult patients with type 2 diabetes in 16 trial sites in Australia. This is a randomized controlled trial enrolling approximately 150 patients into three arms: 1.2mg beloranib, 1.8mg beloranib, and placebo for 52 weeks, followed by an optional open-label treatment extension study where all patients will receive at least six-months treatment with beloranib. Below are the primary and secondary efficacy endpoints:

Primary endpoint:
- Change in body weight

Secondary endpoints:
- Proportion of patients achieving certain change in body weight benchmarks
- Changes in key biomarkers related to glycemic control and other cardio-metabolic parameters

Zafgen expects to report six-month interim data in 4Q15 / 1Q16.

Primary differences of the ZAF-203 Phase IIb trial as compared to the ZAF-201 Phase IIa trials are:

- Trial duration: 52 weeks vs. 12 weeks in ZAF-201
- Different dose: 1.2mg and 1.8mg vs. 0.6mg, 1.2mg, and 2.4mg in ZAF-201
- Requirement for type 2 diabetes as co-morbidity: patients need to have type 2 diabetes (HbA1c of 7% to 11% and fasting glucose <15.5mmol/L) vs. co-morbidity of type 2 diabetes is optional in ZAF-201 (seven of the enrolled 147 patients, or 5% were diabetic).

In the ZAF-201 Phase IIa trial, Zafgen intended to enrich the study population of obesity patients with type 2 diabetes, and the Company had informed trial investigators to enroll this type of patient. However, only seven obese patients with type 2 diabetes were enrolled in the trial. The Company noted that in the ongoing ZAF-203 trial obesity with type 2 diabetes as a co-morbidity was employed as an inclusion criterion to enforce the enrichment for patients of this type.

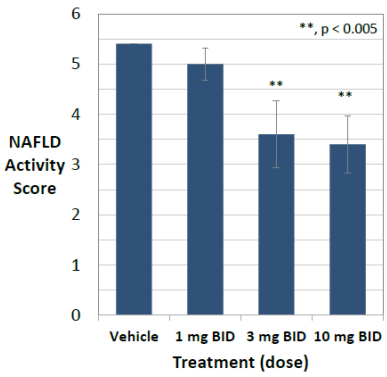
We believe the probability that beloranib meets its primary endpoints in the ZAF-203 trial is high given the similarity between the ZAF-201 Phase IIa trial and the ZAF-203 Phase IIb trial, and the robustness of the efficacy data in the ZAF-201 trial. We believe the higher dose of 1.8mg beloranib should have a better safety and tolerability profile than the 2.4mg dose used in the ZAF-201 trial, but we await the interim data to determine how much of an improvement the lower dose may demonstrate.

ZGN-839 for NASH

Zafgen is developing ZGN-839, an oral MetAP2 inhibitor, for NASH, and is in preparations for an IND submission in mid-2015.

Exhibit 61: Zafgen NASH Program Overview

- **Novel chemical class - potent MetAP2 inhibition**
- **ZGN-839 treatment in mice**
  - Clear target and biomarker activity
  - Promising early safety profile
  - Gene expression profile and animal model efficacy favorable for NASH, fibrosis, and type 2 diabetes
  - ~9% weight loss vs. vehicle after 16 days of treatment
  - Lowers glucose and cholesterol
- **ZGN-839 claimed in multiple patent applications**
- **ZGN-839 in preparation for IND submission –filing anticipated mid-2015**



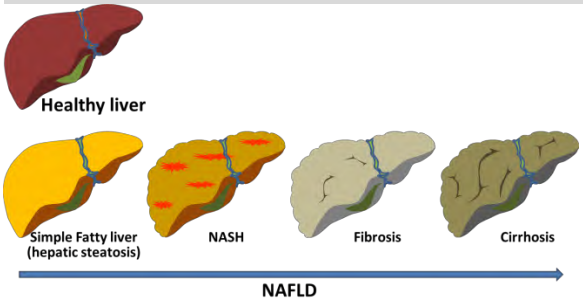
Efficacy in gold standard mouse NASH model after 4 weeks treatment

Source: Zafgen public presentation

NASH is a common and often asymptomatic liver disease with characteristic disease manifestations of fat accumulation and inflammation resulting in damage to the liver. NASH belongs to a larger family of liver diseases collectively named nonalcoholic fatty liver disease (NAFLD), a medical condition that is characterized by the accumulation of fat in liver.

Most NASH patients are asymptomatic. However, NASH is a progressive disease and there is a significant risk of progressing to a more serious state with serious clinical complications such as cirrhosis and hepatocellular carcinoma.

Exhibit 62: The Progression of NAFLD



Source: SunTrust Robinson Humphrey

NASH affects a large percentage of the population. According to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDKD), NASH affects 2% to 5% of people in the U.S. Other epidemiologic studies report a NAFLD prevalence of 10% to 46%, and most biopsy-based studies

confirm a NASH prevalence of 3% to 5% in the U.S. In the rest of the world, NAFLD prevalence is reported to be 6% to 35% with a median of 20%.

The cause(s) and pathogenesis of NASH have not been fully elucidated. A widely accepted theory suggests insulin resistance, a condition in which the body does not respond adequately to insulin in regulating glucose homeostasis, is the key effector leading to NASH.

NASH is a relatively crowded space with many players in clinical or preclinical development. The current leader in the field with regard to the advancement of a clinical program is Intercept Pharmaceuticals with its lead asset obeticholic acid in a large Phase III clinical trial scheduled to enroll a total of 2,500 patients.

Exhibit 63: Summary of NASH Agents in Clinical Development

Drug	Company	Target	Phase	Source
obeticholic acid (OCA)	Intercept Pharmaceuticals, Inc. (ICPT)	Farnesoid X receptor (FXR)/NR1H4	III	Company website
GFT505	Genfit SA (GNFT:FP)	PPAR alpha; PPAR delta	IIb finished	Company website
Aramchol	Galmed Pharmaceuticals Ltd. (GLMD)	ATP-Binding Cassette Transporter 1 (ABCA1); Stearoyl-CoA Desaturase 1 (SCD1)	IIb	Company website
Simtuzumab	Gilead Sciences, Inc. (GILD)	Collagen; Lysyl oxidase-like 2 (LOXL2)	IIb	Company website
Procysbi	Raptor Pharmaceutical Corp. (RPTP)	Lysosomal Cysteine Transporter	IIb	Company website
Cenicriviroc	Tobira Therapeutics (TBRA)	Chemokine Receptor 5 (CCR5); Chemokine Receptor 2 (CCR2)	IIb	Company website
Emricasan	Conatus Pharmaceuticals, Inc. (CNAT)	Caspases	II finished	Company website
Daliresp and Pioglitazone	AstraZeneca PLC (AZN)	Phosphodiesterase 4 (PDE4), PPARγ	II	ClinicalTrials.gov
LCQ908	Novartis AG (NVS)	Diglycerol Acyltransferase (DGAT)	II	ClinicalTrials.gov
Px-104	Gilead (GILD) acquired from Phenex Pharmaceuticals	Farnesoid X receptor (FXR)/NR1H4	II	ClinicalTrials.gov
Remogliflozin etabonate	Islet Sciences, Inc. (ISLT)	SGLT2	IIb expected in 2015	Company website
MSDC-0602	Metabolic Solutions Development Company	Mitochondrial Target of Thiazolidinediones (mTOT)	IIb expected in 2015	Company website
MN-001	MediciNova, Inc. (MNOV)	Leukotriene receptor/Thromboxane receptor	II pending	Company website
A4250	Albireo Pharma	Ileal Bile Acid Transporter (IBAT)/Apical Sodium-dependent Bile Acid Transporter (ASBT)	I	Company website
DUR-928	DURECT Corporation (DRRX)	Unknown, epigenomic regulator program	I	Company website
GR-MD-02	Galectin Therapeutics, Inc. (GALT)	Galectin-3	II expected in 2015	Company website
GS-4997	Gilead Sciences, Inc. (GILD)	Apoptosis Signal Regulating Kinase 1 (ASK1)	I	Company website
NFX-21	Nectid, Inc.	Farnesoid X receptor (FXR)/NR1H4	I	Company website
PXS4728A	Pharmaxis Ltd (PXS:AU)	Semicarbazide-Sensitive Amine Oxidase/Vascular Adhesion Protein-1 (SSAO/VAP-1)	I	Company website
SHP626	Shire Pharmaceuticals Group PLC (SHPG)	Ileal Bile Acid Transporter (IBAT)/Apical Sodium-dependent Bile Acid Transporter (ASBT)	I	ClinicalTrials.gov
NDI-010976	Nimbus Therapeutics	Acetyl-CoA Carboxylase	I	Company website
VBY-376	Virobay, Inc.	Cathepsin B (CTSB)	I	Company website

Source: BiomedTracker, Company website, ClinicalTrials.gov, SunTrust Robinson Humphrey

Zafgen's ZGN-839 has demonstrated encouraging activity in reducing the NAFLD Activity Score (NAS) in the mouse NASH model. The NAFLD Activity Score (NAS) is a grading system used to address the full spectrum of lesions of NAFLD and to assess the severity in clinical trials and natural history studies. The NAS was developed by the Pathology Committee of the NASH Clinical Research Network. The NAS is calculated from three of the four semi-quantitative components: steatosis, lobular inflammation, and hepatocyte ballooning. Each component is assigned a score according to the measures of the specific symptom. The final total score, ranging from 0 to 8, is the un-weighted sum of the biopsy's individual scores for steatosis (0 to 3), lobular inflammation (0 to 3), and hepatocellular ballooning (0 to 2). These three categories are features of active injury that are potentially reversible in the short term. We await clinical data from the ZGN-839 NASH program before including it in our financial model.

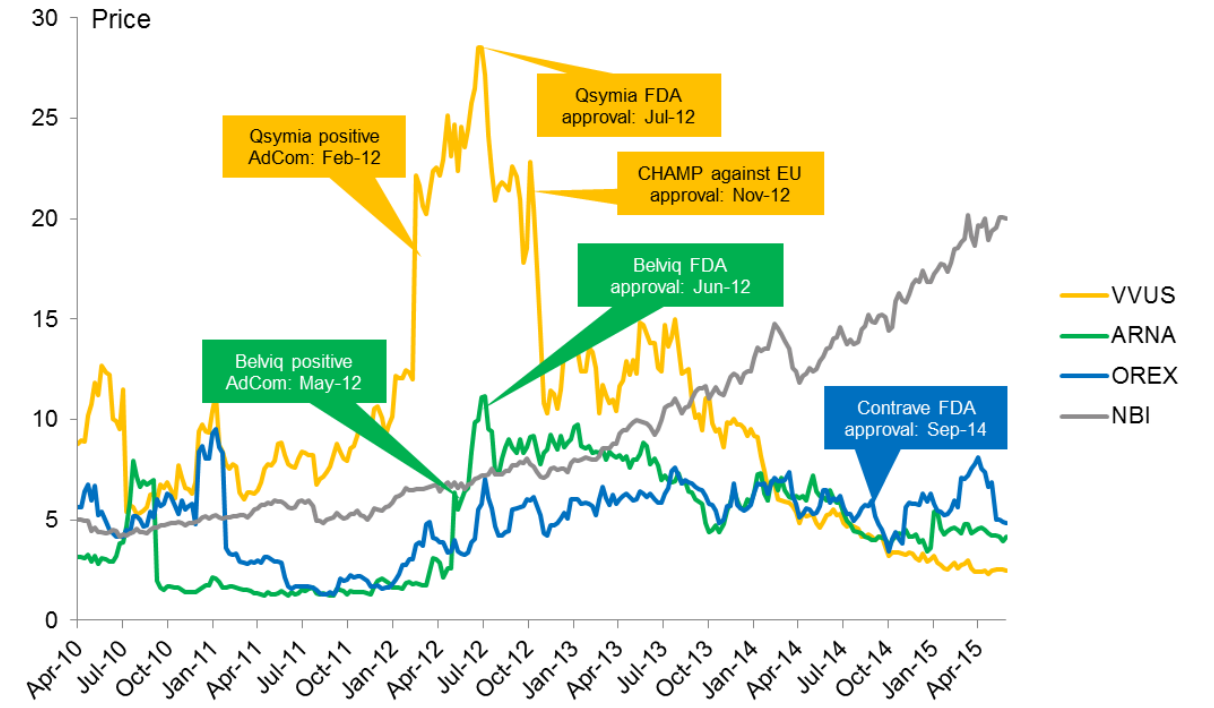
Lesson Learned from the Obesity Space and Why We Believe Beloranib Differentiates

At the Center of the Concern

The obesity space has attracted a lot of investor attention since the late 2000s. However, stock prices for obesity-focused biotech company Vivus and Arena have plummeted since Vivus' Qsymia

and Arena's Belviq received FDA approvals in 2012. All these obesity drugs, also including Orexigen's Contrave approved by the FDA in 2014, failed to deliver stellar returns to investors.

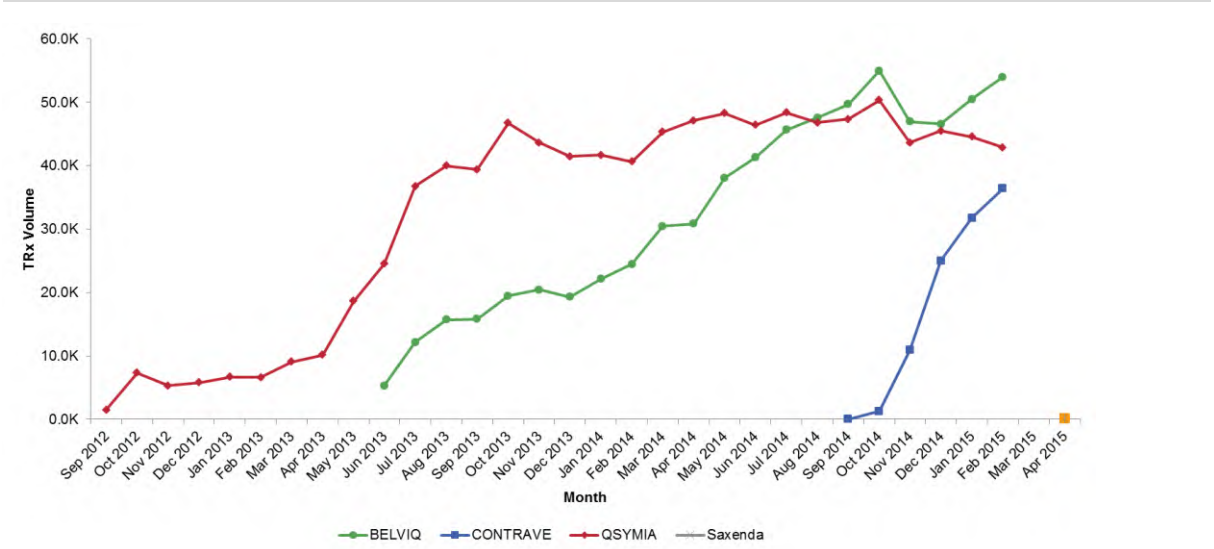
Exhibit 64: Stock Performance and Key Events for VVUS, ARNA and OREX (Apr 2010 – Jun 2015)



Note: NBI, NASDAQ Biotechnology Index;
Source: FactSet, Company websites, SunTrust Robinson Humphrey

A total of 168,000 prescriptions for Qsymia, Belviq and Contrave combined were written in the month of April 2015. A single prescription covers an approximate four-week use period for a patient. Approximately 168,000 obesity patients were on one of these obesity drugs as very few or no patients were on multiple obesity drugs at the same time. According to the CDC, 34.9% or 78.6 million of U.S. adults are obese, who may be eligible for these obesity drugs. Therefore, currently these obesity drugs only penetrate approximately 0.22% (170,000/78.6 million) of the total addressable market in the U.S, which is far below what investors expected prior to regulatory approval.

Exhibit 65: Monthly Total Prescriptions (TRx) of Qsymia, Belviq and Contrave (Sep 2012 – Apr 2015)



Source: IMS, SunTrust Robinson Humphrey

Investors may have concerns that Zafgen shares might follow a similar lackluster path as these other conventional obesity players after receiving regulatory approval. However, we believe ZFGN is differentiated. In the section below we analyze why conventional obesity players have failed to successfully commercialize these obesity drugs and the lessons learned, and why we believe Zafgen is plotted to follow a different course.

Lessons Learned from the Obesity Space

We believe one of the main reasons for the commercialization difficulty of Qsymia/Belviq/Contrave is that prescribing physicians, including endocrinologists, do not view obesity as a disease. Many physicians believe obesity, for the most part, is related to a lack of self-control and can be well managed through lifestyle modification. Physicians, therefore, are hesitant to prescribe obesity medications or only reserve these medications for severely obese patients. Our consultants shared a similar belief and did not view obesity as a disease either. Another important factor hindering the growth of the obesity space is the insufficient level of reimbursement. Although all of the drugs met the primary endpoint of weight reduction, only Orexigen demonstrated a cardiovascular benefit in an outcomes study. As a result, payers hesitated to cover these drugs. The reason for the two-year delay in the FDA's approval of Orexigen's Contrave was due to the time required to complete a cardiovascular outcomes study. Vivus and Arena are also conducting similar studies, as Phase IV trials.

Lack of pharma partnership synergy and/or adequate sales force detailing were not issues. Arena partnered with Eisai and Orexigen partnered with Takeda to commercialize the respective products. A significant cumulative sales force has been deployed: Vivus ~100 sales reps, Eisai ~450 sales reps and Takeda ~900 sales reps. Novo Nordisk plans to use ~500 sales reps. However, the space

is relatively evenly split in terms of prescription numbers, and none of the players dominate the market.

Why We Believe Beloranib is Not Another Obesity Drug

Several points give us confidence in the belief that beloranib is different from conventional obesity drugs:

- Target indication and physician perception of the disease
- The prescriber base
- The novelty of the compounds

A comparison summary and implications to Zafgen are listed in the table below:

Exhibit 66: Comparison between Beloranib and Conventional Obesity Players

	CATEGORY	BELORANIB	CONVENTIONAL OBESITY PLAYERS	IMPLICATION TO ZAFGEN
Different	Indication	Orphan diseases: PWS, HIAO, etc.	Primary care disease: obesity	Ability to charge premium pricing Payer coverage likely more readily
Different	Treating physician	Pediatrician, ped. endocrinologist	Mostly PCP and endocrinologist	Perception of disease and sensitivity to drug pricing different
Different	Physician perception of disease	PWS, HIAO are viewed as diseases	Obesity is not unanimously viewed as disease by physicians	Prescribers are much more willing to prescribe beloranib to treat "real" diseases
Different	Composition of drug	New chemical entity	Qsymia and Contrave are repurposed generic combos	Off-label use largely absent
Different	Route of administration	SubQ twice per week	Oral BID or QD	SubQ is less desirable than oral, but on par with most orphan drugs
Same	Review division within FDA	All drugs reviewed by Division of Metabolism and Endocrinology Products (DMEP) in FDA		Relatively more predictable regarding clinical trial requirement

Source: SunTrust Robinson Humphrey

PWS and HIAO are Considered Diseases; Obesity Not-So-Much

As discussed previously, many physicians, including the physician experts we spoke to, do not view obesity as a disease. Many believe that obesity is largely the result of over-eating, a high-calorie diet, and a lack of exercise, which could and should be managed by the patients themselves. Our consultants, who specialize in pediatric endocrinology and treat PWS and HIAO patients, believe that PWS and HIAO are diseases. PWS and HIAO differ as they have clear etiology of genetic predisposition or result from brain tumor surgery, which are not controllable or manageable by the willpower of PWS and HIAO patients. With this mindset, we believe physicians are more willing to prescribe drugs to PWS and HIAO patients than to general obesity patients.

Pediatricians are Not Endocrinologists

The major prescriber groups for obesity drugs are primary-care physicians and general endocrinologists, while for PWS and HIAO pediatricians or the more specialized pediatric endocrinologists are the main prescribers. We believe pediatricians or pediatric endocrinologists differ from endocrinologists in terms of their prescribing behaviors. Endocrinologists that treat obesity

also treat a large number of diabetes patients. Many of the diabetes drugs are low-priced generics, such as metformin, sulfonylurea, thiazolidinediones (TZD), or non-specialty drugs such as Januvia (cost $4,830 per patient per year based on a dosing of 100mg QD) and Victoza (cost $6,240 per patient per year based on a dosing of 1.2mg QD). We believe endocrinologists might be more sensitive to drug pricing, and less likely to prescribe the relatively expensive obesity drugs.

We believe pediatricians or pediatric endocrinologists who treat PWS or HIAO are familiar and comfortable in prescribing specialty drugs such as human growth hormone (cost $46,000 per patient per year based on a dosing of 1.0 mg/m^2/day, nine-year-old child body surface area of 1.07m^2, and AWP of $882.3 for seven cartridges of Pfizer's Genotropin at 1.0mg per cartridge), which are significantly more costly than the branded drugs endocrinologists prescribe. Our conversations with pediatric endocrinologists confirm that they would readily prescribe PWS or HIAO agents to their patients or at least would not object to trying if the clinical data are robust and payers reimburse the drug, similar to the case of human growth hormone.

Qsymia and Contrave are Mostly Repurposed Generic Combos; Beloranib is a New Molecular Entity

Both Qsymia (phentermine/topiramate extended-release) and Contrave (naltrexone/bupropion) are combinations of two generic drugs.

Phentermine is a psycho-stimulant drug of the phenethylamine class, which can be used as an appetite suppressant. Topiramate is an anti-epileptic drug that inhibits GABA-ergic pathways and glutamate pathways. Naltrexone is an opioid antagonist primarily used in alcohol dependence and opioid dependence management. Bupropion is a non-competitive antagonist of neuronal nicotinic acetylcholine receptors (nAChRs), which is used as an antidepressant and smoking cessation aid.

As Qsymia and Contrave are much pricier than the generic counterparts from which they are created, many obesity patients, especially with poor or those with no insurance coverage, choose to use the combination of generics instead. However, this is not an issue for beloranib as it is a new compound with no generics commercially available.

Overall, we believe that beloranib will not follow the primrose path that the conventional obesity space fell upon. However, how swift the physician adoption is will depend on the final efficacy and safety demonstrated in the pivotal trial, insurance coverage, as well as Zafgen's commercialization capability, which is a question left un-answered to date.

Competitive Landscape

There are no drugs approved for the regulation of hyperphagia or obesity for patients with PWS or HIAO. Growth hormone, such as Genotropin (somatropin [rDNA origin] for injection) is indicated for the treatment of pediatric patients who have growth failure due to genetic PWS confirmed by genetic testing.

Currently three companies besides Zafgen are developing therapeutics for the treatment of hyperphagia or obesity in PWS patients.

Rhythm Metabolic, Inc. (private) is enrolling patients for a Phase II trial to evaluate the effects of a QD SubQ injectable formulation of RM-493, a melanocortin 4 receptor (MC4R) agonist, in obese

subjects with PWS. A total of 36 patients are expected to be enrolled in this 56-days randomized, double blind, placebo-controlled trial with primary endpoints being safety and tolerability of the agent, effect on weight loss, and effect on hyperphagia-related behavior assessed by the PWS Hyperphagia Questionnaire. Rhythm has not yet reported any data with regard to the PWS indication.

Ferring Pharmaceuticals, (private) headquartered in Switzerland, completed a Phase II trial evaluating the effects of FE 992097, or carbetocin which is an analogue of a brain peptide hormone oxytocin, on hyperphagia behaviors in PWS patients. A total of 38 patients were enrolled in this 15-day randomized, double blind, placebo-controlled trial with the primary endpoint being effect on hyperphagia-related behavior assessed by the PWS Hyperphagia Questionnaire. No data have been reported by the Company to date.

Essentialis, Inc. (private) is conducting a Phase I trial evaluating the dosage and tolerability of diazoxide choline controlled-release tablet (DCCR) in patients with PWS. Diazoxide free base is approved as an oral suspension (Proglycem) to treat hypoglycemia caused by certain cancers, surgery, or other conditions. A total of 12 patients will be enrolled in a single-center, open-label, single-arm study with a double-blind, placebo-controlled, randomized withdrawal extension. Patients are initiated on a DCCR dose of 1.5mg/kg and are titrated every 14 days to approximately 2.4mg/kg, 3.3mg/kg, 4.2mg/kg, and 5.1mg/kg (maximum dose of 507.5mg). All patients will be continued in the double-blind, placebo-controlled, randomized withdrawal extension. Any patient who shows an increase in resting energy expenditure and/or a reduction in hyperphagia from baseline through day 55 or day 69 will be designated a responder. Responders will be randomized in a 1:1 ratio either to continue on active treatment at the dose they are treated with on day 69 or to placebo for an additional four weeks. Non-responders will continue open-label treatment during the extension. Primary outcome measures for this trial are hyperphagia using hyperphagia questionnaire, and resting energy expenditure.

With regard to HIAO, Amylin Pharmaceuticals (acquired by AstraZeneca) may be conducting a Phase I/II clinical trial to evaluate exenatide on hypothalamic obesity according to clinicaltrials.gov. However the trial, with a planned duration of six months, started in 2010 and most recently updated in 2013, has not yet released results. We believe it is reasonable to assume that this program has been discontinued or suspended.

Several drugs have been approved for general obesity in the U.S. over the past three years, including Qsymia, Belviq, Contrave and Saxenda. However, they have not been studied in PWS or HIAO. And as discussed previously, the efficacy in PWS or HIAO is not clear since all but Saxenda work via a central mechanism to suppress appetite by targeting pathways in the central nervous system. PWS and HIAO patients, who have an impaired hypothalamus and central nervous system, may theoretically not respond to these obesity drugs.

Intellectual Property Estate

Zafgen owns patents and patent applications covering beloranib's composition of matter, formulations, polymorphs, methods of treating obesity using dosing regimens of beloranib, and methods for treating hypothalamic obesity.

Exhibit 67: Zafgen Patents and Patent Applications

Patent No. or Application No.	Title
Granted Patent	
9,000,035	Treatment of obesity using non-daily administration of 6-O-(4-dimethylaminoethoxy) cinnamoyl fumagillol
8,980,946	Treatment of obesity using non-daily administration of 6-O-(4-dimethylaminoethoxy) cinnamoyl fumagillol
8,865,746	Methods of treating an overweight or obese subject
8,815,309	Methods of treating a subject with benign prostate hyperplasia
8,772,333	Fumigillol type compounds and methods of making and using same
8,735,447	Crystalline solids of a MetAP-2 inhibitor and methods of making and using same
8,642,650	Methods of treating an overweight or obese subject
8,367,721	Methods of treating an overweight or obese subject
8,349,891	Crystalline solids of a MetAP-2 inhibitor and methods of making and using same
Patent Application	
20150126489	Fumigillol Compounds and Methods of Making and Using Same
20150111964	Polymorphic Salt of a MetAP-2 Inhibitor and Methods of Making and Using Same
20150111963	Fumigillol Type Compounds and Methods of Making and Using Same
20150018413	Crystalline Solids of a METAP-2 Inhibitor and Methods of Making and Using Same
20140378462	Tricyclic Sulfonamide Compounds and Methods of Making and Using Same
20140336251	Methods of Treating Age Related Disorders
20140155348	Inclusion Compounds of Fumagillol Derivative or its Salt, and Pharmaceutical Compositions Comprising the
20140107171	Methods of Treating an Overweight or Obese Subject
20140088078	Partially Saturated Tricyclic Compounds and Methods of Making and Using Same
20140080822	Tricyclic Pyrazole Sulphonamide Compounds and Methods of Making and Using Same
20140073691	Methods and composition for Treating Thyroid Hormone Related Disorders
20140073623	Tricyclic Sulfonamide Compounds and Methods of Making and Using Same
20140051752	Treatment of Obesity Using Non-Daily Administration of 6-O-(4-Dimethylaminoethoxy) Cinnamoyl Fumagillol
20140045934	Treatment of Obesity Using Non-Daily Administration of 6-O-(4-Dimethylaminoethoxy) Cinnamoyl Fumagillol
20140011870	Methods of Treating Obesity Using an Effective Dose of a METAP-2 Inhibitor
20130331420	Tetrazole Compounds and Methods of Making And Using Same
20130316994	Methods of Reducing Risk of Hepatobiliary Dysfunction During Rapid Weight Loss with METAP-2 Inhibitors
20130217759	Sulphonamine Compounds and Methods of Making and Using Same
20100016425	Methods of Treating an Overweight or Obese Subject

Source: USPTO, SunTrust Robinson Humphrey

Zafgen expects that the U.S. and EU patents covering beloranib's compositions of matter will expire in 2019. Two issued U.S. patents covering beloranib polymorph's composition of matter will expire in 2031 and two issued U.S. patents covering methods of treating obesity will expire in 2029. Zafgen owns pending patent applications in Europe related to beloranib polymorph composition of matter and methods of treating obesity that the Company expects to expire in 2031 if issued. Zafgen noted in the 4Q14 earnings call that a patent covering the twice-weekly dose regimen for beloranib was granted by the USPTO. This patent will expire in 2029.

Manufacturing and Commercialization

Zafgen currently has no manufacturing facilities and relies on contract manufacturers to produce beloranib for clinical trials. Zafgen has not yet established long-term supply agreements with its contractors, and each batch is individually contracted under a quality and supply agreement. The Company noted that current scale of manufacturing was adequate to support clinical trial supplies and launch for Orphan indications.

Zafgen previously used a two-vial system with single use glass vials for beloranib which will potentially be replaced by a pre-filled diluent syringe after the ZAF-311 trial.

Zafgen does not currently have any internal sales, marketing or distribution infrastructure given the pre-commercial stage nature of the clinical pipeline. The Company plans to commercialize beloranib

in the U.S. and EU on a go-it-alone strategy. The Company is evaluating partnering opportunities for Asia/ROW. The sales force for US/EU for PWS/HIAO will require a small, focused sales force given the niche of physicians being targeted.

Management and Compensation

We believe Zafgen has built a seasoned management team with extensive experience in the development and commercialization of therapeutics for the treatment of obesity as well as Orphan diseases.

Management

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

Dr. Hughes has served as Zafgen's CEO and a member of the Board of Directors since October 2008. From October 2008 until June 2014, Dr. Hughes also served as President. From 1987 to 2008, he 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, where he oversaw drug discovery and development projects targeting obesity, diabetes and heart disease. Dr. Hughes authored over 40 publications and invented patents related to the treatment of diabetes, cardiovascular disease and obesity. Dr. Hughes received a Ph.D. in nutritional biochemistry from Tufts University and a B.A. in biology from Franklin and Marshall College.

Patrick Loustau, President

Mr. Loustau has served as Zafgen's President since June 2014. From August 2010 to April 2014, Mr. Loustau served as SVP for Global Commercialization in Cardiovascular & Metabolics at Bristol-Myers Squibb. From May 1996 to July 2010, he held roles as SVP for Global Marketing & Medical Affairs, VP, Sales Force and Managed Care/Government Affairs, President & GM (Toronto), Regional Business Directors Sales and Senior Director Marketing Diabetes and Project Leader-Business Acceleration at Novo Nordisk. Mr. Loustau started his career with Parke-Davis as an HR and Training Manager in 1989. Mr. Loustau holds a Maitrise in Physiology from the University Paris-XI in Orsay, a DEA in Psychology from the University Paris-X in Nanterre and a DESS in Human Resources and Marketing from the Enterprise Administration Institute in Bordeaux.

Patricia L. Allen, Chief Financial Officer

Ms. Allen has served as Zafgen's CFO since January 2013. From 2011 to 2012, Ms. Allen 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. From 2004 to 2011, Ms. Allen served as the Vice President of Finance, Treasurer and Principal Financial Officer of Alnylam Pharmaceuticals, where she interacted with the investment community and was influential in raising over $900 million via the company's initial public offering, follow-on common stock offerings and multiple business development transactions. Prior to Alnylam, Ms. Allen worked at Alkermes, Inc., most recently as the Director of Finance. Ms. Allen began her career as an auditor at Deloitte & Touche, LLP. Ms. Allen graduated summa cum laude from Bryant College with a B.S. in business administration.

Dennis D. Kim, M.D., MBA, Chief Medical Officer

Dr. Kim has served as Zafgen's CMO since September 2011. From 2001 to 2012, Dr. Kim was an assistant professor of medicine, division of endocrinology/metabolism, at the University of California, San Diego School of Medicine. From September 2008 to February 2011, Dr. Kim held multiple senior-level clinical and corporate affairs positions at Orexigen Therapeutics, including Senior Vice President, Dead of Obesity/metabolic Diseases; Senior Vice President, corporate development; and Senior Vice President, medical affairs and communications. Prior to Orexigen, from September 2007 to September 2008, he was CMO and Vice President of medical affairs at EnteroMedics, where he oversaw clinical affairs and successfully implemented an initial public offering as part of the executive team in 2007. Previously, from July 2001 to September 2007, he held positions of increasing responsibility at Amylin Pharmaceuticals, Inc., most recently as Executive Director, corporate strategy, where he managed corporate and business strategic planning spanning all commercial products, developmental drug candidates, corporate alliance partnership and manufacturing support. Dr. Kim holds an M.D. from the University of Health Sciences, The Chicago Medical School, an MBA from University of California, San Diego Rady School of Management, and a B.S. in biology from the University of California at Los Angeles.

Alicia Secor, Chief Commercial Officer

Ms. Secor has served as Zafgen's CCO since January 2014. From August 2013 to October 2013, she served as Senior Vice President and Chief Operating Officer of Synageva BioPharma Corp.. Previously, from November 1998 to July 2013, Ms. Secor spent 15 years at Genzyme Corporation, where she held various leadership positions, most recently as Vice President and General Manager of Metabolic Diseases. Prior to this role, she was Vice President and General Manager of Biosurgical Specialties, a surgical device business focused on adhesion prevention and other novel applications for biomaterials. During her tenure at Genzyme, she was instrumental in advancing products through clinical development and responsible for establishing and executing the commercial development and launch, general management and global expansion. Prior to Genzyme, Ms. Secor held positions at Alkermes in business development, at Centocor, Inc. (a Johnson & Johnson Company) in clinical and commercial operations, and began her career at Pfizer Inc. as a hospital-based sales representative. She received her MBA from Northeastern University, and her B.S. in Healthcare Administration from the University of New Hampshire.

Compensation

Zafgen's compensation committee members are independent and have not been employed by Zafgen over the past three years. The compensation committee made all compensation decisions with regard to the executive officers. The executive compensation consists of base salary, cash incentive bonuses, long-term incentive compensation which includes restricted common stock, restricted stock units and stock options and broad-based benefits programs. We believe Zafgen's executive compensation is fair and aligned with shareholders' interests. Over 70% of Patrick Loustau and Alicia Secor's 2014 compensations are in the form of option awards. CEO Thomas Hughes is eligible for an annual merit bonus with a target bonus of 35% of his base salary, and he owns 508,086 shares or 1.9% of the total shares outstanding. All of the compensation programs provide a strong incentive to Zafgen management to achieve short-term and long-term goals and to add value for shareholders.

Exhibit 68: Summary of Compensation for Zafgen Officers - 2014 and 2013 Fiscal Years

Name and Principal Position	Year	Salary ($)	Option Awards ($)	Non-Equity Incentive Plan Compensation ($)	All Other Compensation ($)	Total ($)
Thomas E. Hughes, Ph.D.	2014	425,000	—	178,500	5,200	608,700
Chief Executive Officer	2013	400,000	591,961	120,000	5,100	1,117,061
Patrick Loustau	2014	195,385	3,379,818	70,000	29,332	3,674,535
President						
Alicia Secor	2014	328,750	1,161,651	99,000	5,200	1,594,601
Chief Commercial Officer						

Source: Company filings

Appendix: Abbreviations and Acronyms Used in the Report

BID	twice a day
BIW	twice a week
BMI	body mass index
BP	blood pressure
DCCR	diazoxide choline controlled-release
DCF	discounted cash flow
DEXA	dual-energy x-ray absorptiometry
ERK	extracellular signal-regulated kinases
EV	enterprise value
FDA	Food and Drug Administration
FGF	fibroblast growth factor
FISH	fluorescence in-situ hybridization
hGH	human growth hormone
HIAO	hypothalamic injury associated obesity
IV	intravenous
MC4R	melanocortin 4 receptor
MetAP2	methionine aminopeptidase 2
MOA	mechanism of action
MTD	maximum tolerated dose
nAChR	neuronal nicotinic acetylcholine receptor
NAFLD	nonalcoholic fatty liver disease
NAS	NAFLD Activity Score
NASH	nonalcoholic steatohepatitis

NIDDKD	National Institute of Diabetes and Digestive and Kidney Diseases
NIH	National Institutes of Health
NPV	net present value
PWS	Prader-Willi syndrome
PWS-HQ	PWS Hyperphagia Questionnaire
QD	once a day
QW	once a week
SAE	severe adverse event
SRC	Safety Review Committee
SREBP	sterol regulatory element binding protein
SubQ	subcutaneous
TEAT	treatment-emergent adverse event
TZD	thiazolidinedione
UPD	uniparental disomy
VAS	visual analogue scale

Zafgen's Quarter P&L Model ($MM)

	2011A	2012A	2013A	Q1:14A	Q2:14A	Q3:14A	Q4:14A	2014A	Q1:15A	Q2:15E	Q3:15E	Q4:15E	2015E
Revenues													
Total U.S. sales revenue for PWS booked by Zafgen ($MM)	-	-	-	-	-	-	-	-	-	-	-	-	-
Total EU sales revenue for PWS booked by Zafgen ($MM)	-	-	-	-	-	-	-	-	-	-	-	-	-
Total WW revenue booked by Zafgen for beloranib in PWS ($MM)	-	-	-	-	-	-	-	-	-	-	-	-	-
Total U.S. sales revenue for HIAO booked by Zafgen ($MM)	-	-	-	-	-	-	-	-	-	-	-	-	-
Total EU sales revenue for HIAO booked by Zafgen ($MM)	-	-	-	-	-	-	-	-	-	-	-	-	-
Total WW revenue booked by Zafgen for beloranib in HIAO ($MM)	-	-	-	-	-	-	-	-	-	-	-	-	-
Total WW revenue booked by Zafgen for beloranib in PWS and HIAO ($MM)													
Royalties paid to Chong Kun Dang Pharmaceutical													
Royalties paid to Children's Medical Center													
Operating Expenses													
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Research and Development	11.4	11.5	9.6	3.3	4.7	12.1	7.3	27.4	10.2	15.0	15.5	16.0	56.7
General and Administrative	1.8	2.2	4.2	1.2	1.3	2.3	3.3	8.1	3.0	5.0	5.2	5.3	18.5
Sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Operating Expenses	**13.2**	**13.8**	**13.8**	**4.5**	**6.0**	**14.4**	**10.7**	**35.5**	**13.2**	**20.0**	**20.7**	**21.3**	**75.2**
Operating Income (Loss)	**(13.2)**	**(13.8)**	**(13.8)**	**(4.5)**	**(6.0)**	**(14.4)**	**(10.7)**	**(35.5)**	**(13.2)**	**(20.0)**	**(20.7)**	**(21.3)**	**(75.2)**
Other non-operating income (loss)													
Interest income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest expense	0.0	(0.1)	0.0	(0.0)	(0.4)	(0.2)	(0.2)	(0.9)	(0.2)	0.0	0.0	0.0	0.0
Foreign currency transaction gains (losses), net	(0.0)	0.0	(0.2)	0.1	0.0	(0.1)	(0.1)	(0.1)	(0.1)	0.0	0.0	0.1	0.0
Total other income (expense), net	**(0.0)**	**(0.1)**	**(0.2)**	**0.1**	**(0.4)**	**(0.3)**	**(0.3)**	**(0.9)**	**(0.2)**	**0.0**	**0.0**	**0.1**	**0.0**
Income (Loss) before tax	**(13.2)**	**(13.9)**	**(14.0)**	**(4.5)**	**(6.4)**	**(14.7)**	**(10.9)**	**(36.5)**	**(13.5)**	**(20.0)**	**(20.7)**	**(21.3)**	**(75.2)**
Accretion of redeemable convertible preferred stock to redemption value	(0.1)	(0.1)	(0.2)	(0.0)	(0.0)	0.0	0.0	(0.1)	0.0	0.0	0.0	0.0	0.0
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Income Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net income (loss) attributable to common stockholders	(13.2)	(13.9)	(14.2)	(4.5)	(6.4)	(14.7)	(10.9)	(36.6)	(13.5)	(20.0)	(20.7)	(21.3)	(75.2)
Net Income (Loss) per share - basic and diluted	**($19.17)**	**($19.64)**	**($19.53)**	**($6.11)**	**($2.96)**	**($0.65)**	**($0.47)**	**($3.00)**	**($0.50)**	**($0.73)**	**($0.74)**	**($0.75)**	**($2.72)**
Weighted average common shares outstanding - basic and diluted	0.7	0.7	0.7	0.7	2.2	22.7	23.1	12.2	26.9	27.4	28.0	28.5	27.7

Source: Zafgen public filings, SunTrust Robinson Humphrey

Zafgen's Annual P&L Model ($MM)

	2011A	2012A	2013A	2014A	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E
Revenues															
Total U.S. sales revenue for PWS booked by Zafgen ($MM)	-	-	-	-	-	-	-	10.3	182.4	315.7	422.6	510.3	561.5	616.9	652.4
Total EU sales revenue for PWS booked by Zafgen ($MM)	-	-	-	-	-	-	-	6.1	123.3	175.4	210.4	249.3	288.6	331.2	348.4
Total WW revenue booked by Zafgen for beloranib in PWS ($MM)	-	-	-	-	-	-	-	16.4	305.8	491.1	633.1	759.7	850.1	948.1	1,000.8
Total U.S. sales revenue for HIAO booked by Zafgen ($MM)	-	-	-	-	-	-	-	-	-	39.8	56.1	89.0	109.8	124.4	140.4
Total EU sales revenue for HIAO booked by Zafgen ($MM)	-	-	-	-	-	-	-	-	-	32.8	41.5	72.7	91.8	104.6	118.6
Total WW revenue booked by Zafgen for beloranib in HIAO ($MM)	-	-	-	-	-	-	-	-	-	72.7	97.6	161.7	201.6	229.1	258.9
Total WW revenue booked by Zafgen for beloranib in PWS and HIAO ($MM)								**16.4**	**305.8**	**563.7**	**730.7**	**921.4**	**1,051.7**	**1,177.2**	**1,259.7**
Royalties paid to Chong Kun Dang Pharmaceutical								0.5	9.2	16.9	21.9	27.6	31.6	35.3	37.8
Royalties paid to Children's Medical Center								0.3	6.1	11.3	14.6	18.4	21.0	23.5	25.2
Operating Expenses															
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.5	45.9	84.6	109.6	138.2	157.8	176.6	189.0
Research and Development	11.4	11.5	9.6	27.4	56.7	79.4	100.0	120.0	130.0	135.0	146.1	184.3	210.3	235.4	251.9
General and Administrative	1.8	2.2	4.2	8.1	18.5	19.9	25.0	30.0	32.5	33.8	36.5	46.1	52.6	58.9	63.0
Sales	0.0	0.0	0.0	0.0	0.0	0.0	5.0	10.0	25.0	35.0	40.0	45.0	50.0	55.0	60.0
Total Operating Expenses	**13.2**	**13.8**	**13.8**	**35.5**	**75.2**	**99.3**	**130.0**	**162.5**	**233.4**	**288.3**	**332.3**	**413.6**	**470.7**	**525.9**	**563.9**
Operating Income (Loss)	**(13.2)**	**(13.8)**	**(13.8)**	**(35.5)**	**(75.2)**	**(99.3)**	**(130.0)**	**(146.9)**	**57.1**	**247.2**	**361.9**	**461.8**	**528.4**	**592.5**	**632.9**
Other non-operating income (loss)															
Interest income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Interest expense	0.0	(0.1)	0.0	(0.9)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Foreign currency transaction gains (losses), net	(0.0)	0.0	(0.2)	(0.1)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total other income (expense), net	**(0.0)**	**(0.1)**	**(0.2)**	**(0.9)**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
Income (Loss) before tax	**(13.2)**	**(13.9)**	**(14.0)**	**(36.5)**	**(75.2)**	**(99.3)**	**(130.0)**	**(146.9)**	**57.1**	**247.2**	**361.9**	**461.8**	**528.4**	**592.5**	**632.9**
Accretion of redeemable convertible preferred stock to redemption value	(0.1)	(0.1)	(0.2)	(0.1)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Tax rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*8%*	*12%*	*18%*	*27%*	*35%*	*35%*	*35%*
Income Tax	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	4.6	29.7	65.1	124.7	185.0	207.4	221.5
Net income (loss) attributable to common stockholders	(13.2)	(13.9)	(14.2)	(36.6)	(75.2)	(99.3)	(130.0)	(146.9)	52.5	217.6	296.7	337.1	343.5	385.1	411.4
Net Income (Loss) per share - basic and diluted	**($19.17)**	**($19.64)**	**($19.53)**	**($3.00)**	**($2.72)**	**($2.96)**	**($3.69)**	**($3.65)**	**$1.24**	**$4.91**	**$6.37**	**$6.90**	**$6.69**	**$7.15**	**$7.27**
Weighted average common shares outstanding - basic and diluted	0.7	0.7	0.7	12.2	27.7	33.5	35.2	40.2	42.2	44.3	46.6	48.9	51.3	53.9	56.6

Source: Zafgen public filings, SunTrust Robinson Humphrey

Company Description

Zafgen is a clinical stage biopharmaceutical company developing treatments for rare obesity diseases including Prader-Willi syndrome (PWS) and hypothalamic injury associated obesity (HIAO), as well as severe and complicated obesity. Zafgen has completed six placebo controlled human clinical trials with promising data and is conducting two clinical trials for its lead product candidate beloranib, an inhibitor of MetAP2, an enzyme that modulates the activity of key cellular processes that control metabolism. Zafgen is conducting a Phase III trial for beloranib in PWS with top-line data expected in 1Q16 and a Phase IIb trial for beloranib in severe and complicated obesity with interim data expected in 4Q15/1Q16. Zafgen was founded in November 2005 and is headquartered in Boston, MA. The Company completed an IPO in June 2014.

Investment Thesis

We view Zafgen as a differentiated and attractive clinical stage biotechnology play in the Orphan obesity space and potentially the much larger size metabolism markets with its lead asset beloranib. Beloranib has the potential to address hyperphagia and obesity in Prader-Willi syndrome (PWS) and hypothalamic injury associated obesity (HIAO). These two symptoms represent significant unmet medical needs according to our pediatric endocrinology consultants and there has been no FDA approved drugs to date. Zafgen has completed six randomized placebo-controlled clinical trials in over 250 patients for beloranib for three indications related to obesity: PWS, HIAO, and severe/complicated obesity. Results to date have demonstrated clinically meaningful efficacy and a benign safety profile. Despite several changes from previously conducted trials with regard to design, we believe a high probability of success for the ongoing ZAF-311 Phase III trials for beloranib in PWS. Top-line data for the six-month randomized period is expected by 1Q16 and is the most imminent and impactful catalyst for Zafgen shares. Our deep dive in the obesity space suggests that commercialization issues, which have plagued other conventional obesity players, should not be an overhang for Zafgen.

Valuation and Risks

Our price target of $47 is derived from an average of three different valuation methodologies. We attain a 12-month price target of $44.9 with a discounted earnings model, a price target of $47.6 with a discounted cash flow model, and a price target of $47.7 with a clinical net present value model. Details of these models are contained within this report.

The primary risks associated with an investment in Zafgen include the following:

Clinical risk: While beloranib has accumulated consistent and promising data over the six completed clinical trials and we believe beloranib has a high likelihood of success in the ongoing ZAF-311 Phase III bestPWS trial for the treatment of PWS; there is no guarantee of success. The change in trial duration and dosage, and the employment of co-primary endpoints as compared to the ZAF-211 Phase IIa trial, are uncertainties.

Regulatory risk: Despite the promising data from clinical trials to date, there is no guarantee that future clinical trials will also be successful and that the FDA will approve beloranib. The FDA's requirement of co-primary endpoints should raise the bar for approval; but the Agency lowered the bar by reducing the required level of statistical significance to p <0.05 from p <0.025, which net-net could potentially increase or decrease the bar for approval. Our understanding is that the FDA has not signed off as to the required level of weight reduction as compared to placebo in the Phase III ZAF-311 trial, which could be an uncertainty.

Commercial risk: Zafgen has not previously launched or marketed a commercial product. In order to successfully commercialize beloranib, Zafgen needs to establish a salesforce as well as secure payer coverage for beloranib. The formulary decision is based on not only the clinical data, but also on the pricing of beloranib among other factors, which is currently unknown variables. Should beloranib fail to be covered, we expect it will significantly diminish beloranib's commercial prospects.

Companies Mentioned in This Note

Galmed Pharmaceuticals Ltd (GLMD, $10.21, Buy)
Pfizer Inc. (PFE, $34.04, Reduce)
Shire plc (SHPG, $243.88, Buy)
Arena Pharmaceuticals, Inc. (ARNA $4.23 NR)
AstraZeneca PLC Sponsored ADR (AZN $64.99 NR)
DURECT Corporation (DRRX $2.8 NR)
Eisai Co., Ltd. Sponsored ADR (ESALY $64.157 NR)
Galectin Therapeutics Inc. (GALT $3.17 NR)

Gilead Sciences, Inc. (GILD $118.16 NR)
Genfit SA (GNFTF $38.44 NR)
Intercept Pharmaceuticals, Inc. (ICPT $244.36 NR)
Islet Sciences, Inc. (ISLT $0.1445 NR)
MediciNova, Inc. (MNOV $4.04 NR)
Novo Nordisk A/S Sponsored ADR (NVO $56.23 NR)
Novartis AG Sponsored ADR (NVS $100.11 NR)
Pfizer Inc. (PFE $34.04 NR)
Pharmaxis Ltd (PXS:AU 0.23AUD NR)
Raptor Pharmaceutical Corp. (RPTP $14.57 NR)
Shire PLC Sponsored ADR (SHPG $243.88 NR)
Tobira Therapeutics, Inc. (TBRA $20.51 NR)
Takeda Pharmaceutical Co. Ltd. Sponsored ADR (TKPYY $24.79 NR)
VIVUS, Inc. (VVUS $2.48 NR)
Rhythm Metabolic, Inc. (private)
Ferring Pharmaceuticals (private)
Essentialis, Inc. (private)

Analyst Certification

I, Edward Nash , hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities. I also certify that I have not been, am not, and will not be receiving direct or indirect compensation in exchange for expressing the specific recommendation(s) in this report.

Required Disclosures

SunTrust Robinson Humphrey, Inc. makes a market in the following companies at the time of this report: GLMD, SHPG, ZFGN-US

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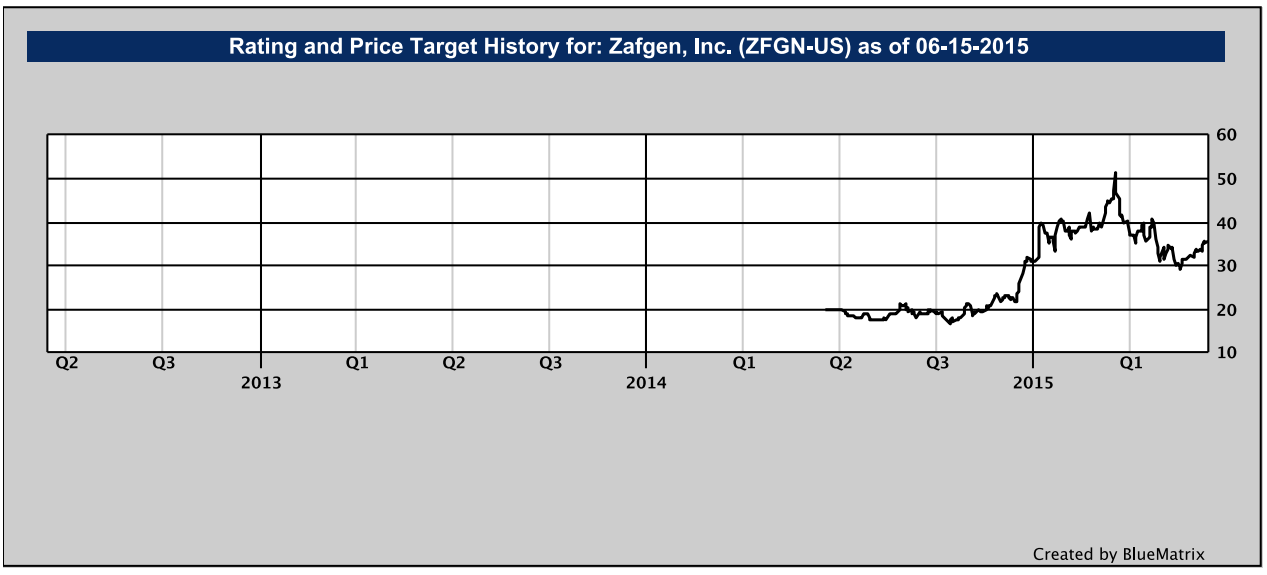

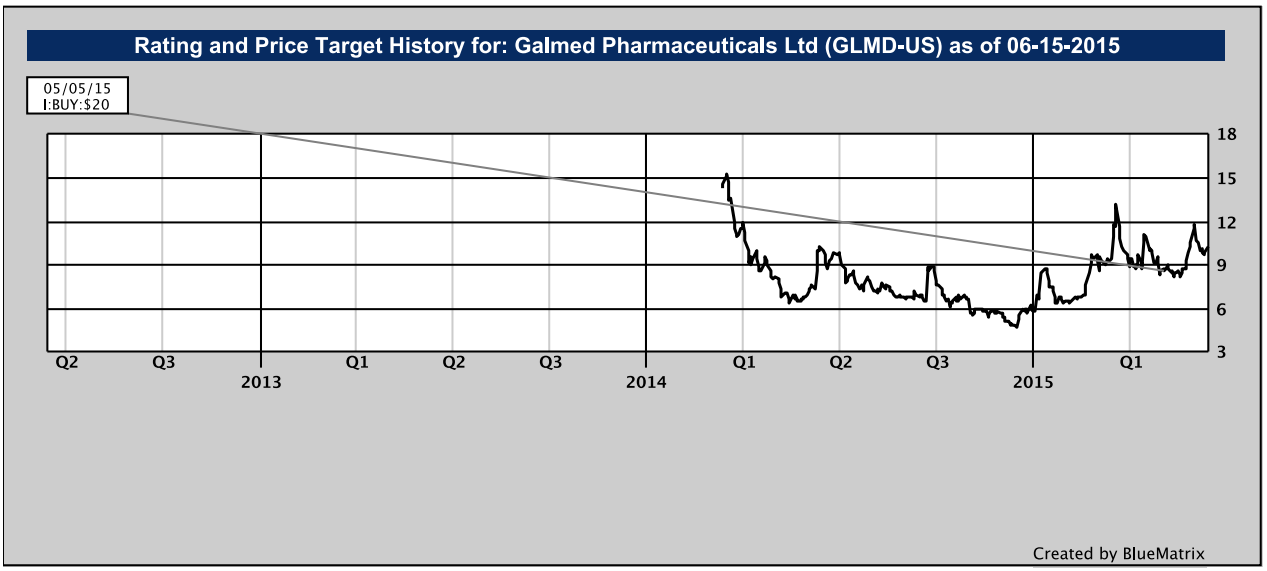
Rating and Price Target History for: Galmed Pharmaceuticals Ltd (GLMD-US) as of 06-15-2015
05/05/15
I:BUY:$20
18
15
12
9
6
3
Q2
Q3
Q1
Q2
Q3
Q1
Q2
Q3
Q1
2013
2014
2015
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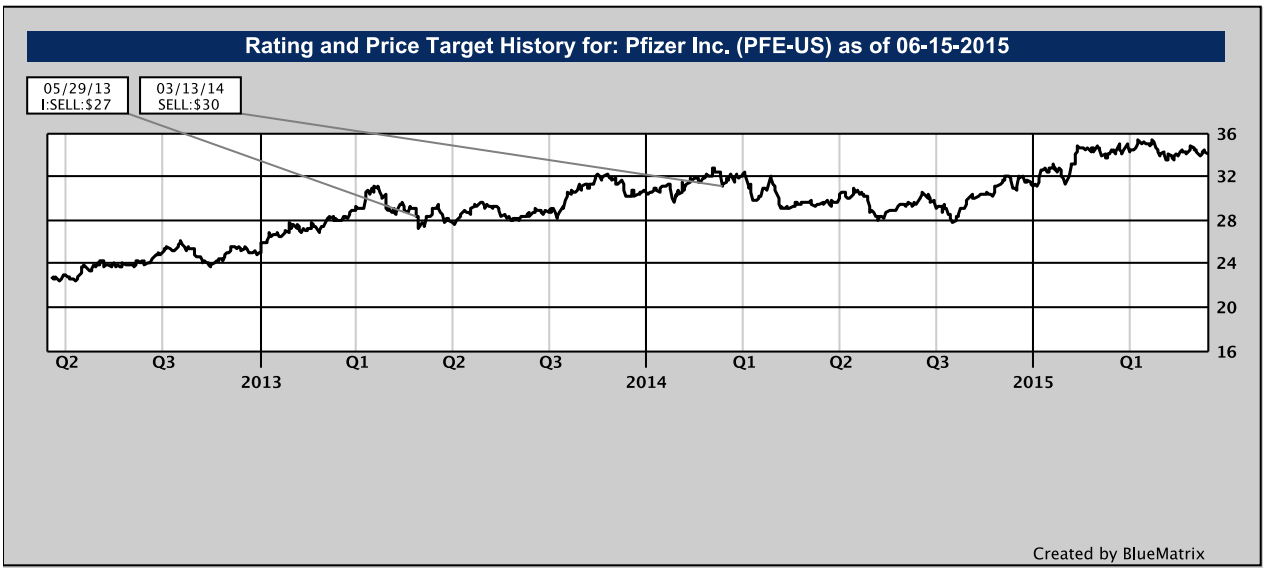
Rating and Price Target History for: Pfizer Inc. (PFE-US) as of 06-15-2015
05/29/13
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03/13/14
SELL:$30
36
32
28
24
20
16
Q2
Q3
Q1
Q2
Q3
Q1
Q2
Q3
Q1
2013
2014
2015
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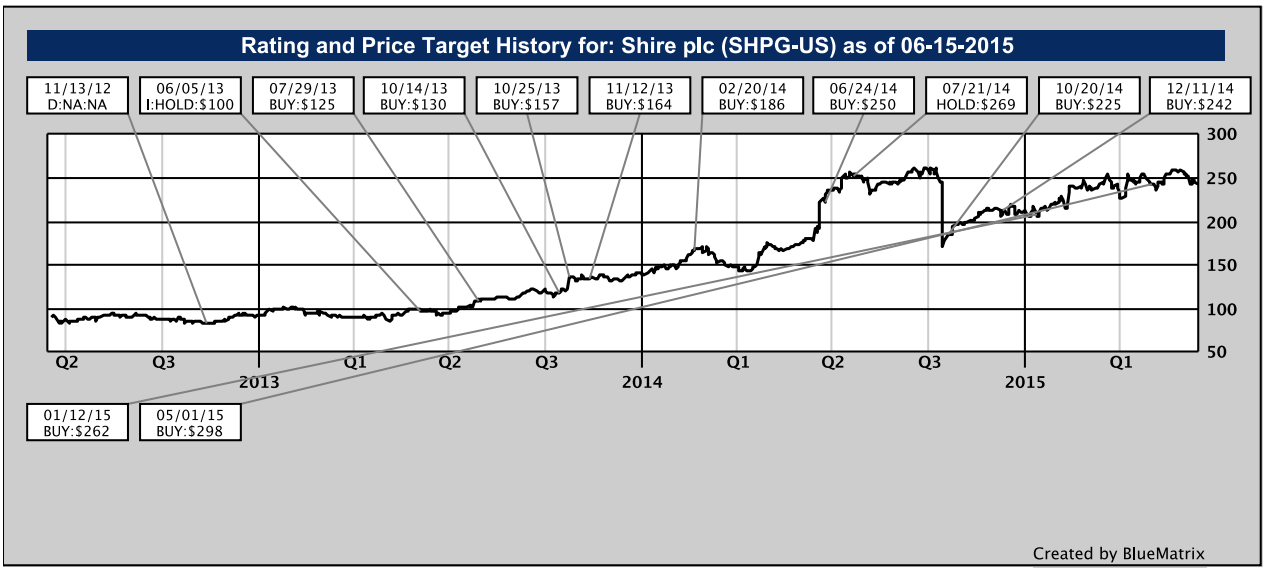

STRH Ratings System for Equity Securities

3 designations based on total returns* within a 12-month period**

- **Buy** – total return ≥ 15% (10% for low-Beta securities)***
- **Reduce** – total return ≤ negative 10% (5% for low Beta securities)
- **Neutral** – total return is within the bounds above
- **NR** – NOT RATED, STRH does not provide equity research coverage
- **CS** – Coverage Suspended

*Total return (price appreciation + dividends)
**Price targets are within a 12-month period, unless otherwise noted
***Low Beta defined as securities with an average Beta of 0.8 or less, using Bloomberg's 5-year average Beta

Legend for Rating and Price Target History Charts:
D = drop coverage
I = initiate coverage
T = transfer coverage

SunTrust Robinson Humphrey ratings distribution (as of 06/16/2015):

Coverage Universe			Investment Banking Clients Past 12 Months		
Rating	**Count**	**Percent**	**Rating**	**Count**	**Percent**
Buy	304	53.62%	Buy	112	36.84%
Neutral	257	45.33%	Neutral	53	20.62%
Sell/Reduce	6	1.06%	Sell/Reduce	1	16.67%

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