EQUITY RESEARCH INITIATION

RBC Capital Markets

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Zafgen, Inc.

Initiating with Outperform: This is not your father's obesity drug

Our view: Early studies of injectable agent beloranib in obese patients resulted in impressive weight loss. Zafgen, however, plans a faster path to market, by testing beloranib in Prader-Willi Syndrome (PWS), an obesity-related, rare disease. We expect positive Phase III data in PWS YE15, and if approved, $750MM in peak 2029 WW sales in PWS alone, with the hypothalamic injury-associated obesity (HIAO) indication right behind it.

Key points:

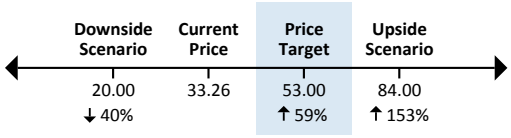
A really impressive injectable drug for obesity… Beloranib acts via a novel mechanism of action (MOA) to lead to rapid and impressive weight loss in the obese patients it has been tested on in early stage Phase I and II trials. Using a different MOA than the ones used by the weight loss drugs currently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

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

Prader-Willi Syndrome: a rare, genetic, obesity-related disease. There are an estimated 21,000 PWS cases in the US, with 7,500 of them identified. PWS patients are characterized by hyperphagia, the inability to feel hunger, which leads them to overeat and (most) to become obese. After promising data from a 17-patient Phase II trial, Zafgen is testing the drug in the bestPWS Phase III trial, with data expected YE15. A second trial to be conducted in Europe is expected to start soon, and will be required for US and EU approval. Based on the efficacy observed thus far, we expect the Phase III program to be successful, and the drug to be approved. Zafgen plans to market beloranib on its own, via a specialty salesforce, and we project that it can become a significant product in PWS alone, reaching $750MM in peak US/EU 2029 sales.

HIAO doubles beloranib's commercial potential: Zafgen recently reported positive data from a 14-patient, Phase II trial of beloranib in patients with hypothalamic injury-associated obesity (HIAO). These patients develop obesity due to uncontrollable hunger, somewhat akin to an "acquired PWS", following surgery to remove craniopharyngiomas. Positive pivotal data in this setting would make HIAO the second rare disease indication for beloranib, doubling its market potential.

Outperform
Speculative Risk
NASDAQ: ZFGN; USD 33.26
Price Target USD 53.00
Scenario Analysis*



*Implied Total Returns

Key Statistics

Shares O/S (MM):	27.8	Market Cap (MM):	925
Dividend:	0.00	Yield:	0.0%
		Avg. Daily Volume:	139,481

RBC Estimates

FY Dec	2014E	2015E	2016E
Revenue	0.0	0.0	0.0
EPS, Ops Diluted	(2.90)	(1.55)	(1.45)

Revenue	Q1	Q2	Q3	Q4
2014	0.0A	0.0A	0.0A	0.0E
2015	0.0E	0.0E	0.0E	0.0E
EPS, Ops Diluted				
2014	(6.18)A	(2.96)A	(0.65)A	(0.41)E
2015	(0.37)E	(0.38)E	(0.39)E	(0.41)E

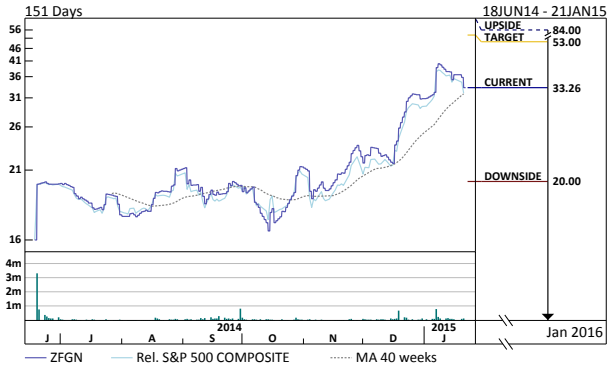
All values in USD unless otherwise noted.

Priced as of prior trading day's market close, EST (unless otherwise noted).

For Required Conflicts Disclosures, see Page 43

Target/Upside/Downside Scenarios

Exhibit 1: Zafgen, Inc.



Source: Bloomberg and RBC Capital Markets estimates for Upside/Downside/Target

Target price/base case

To value ZFGN shares at $53, we use a sum-of-the-parts methodology, and estimate the probability adjusted NPV of the following: 1) beloranib sales in PWS ($30/share), 2) beloranib sales in HIAO ($17/share), and 3) the company's projected net cash position (~$6/share). We assign a probability of success of 60% for PWS and 50% for HIAO, and model peak US/EU sales of beloranib in PWS and HIAO of $750MM and $630MM, respectively.

Upside scenario

Our upside scenario of $84/share assumes positive data from the Phase IIb trial of beloranib in severe obesity, an indication which is currently not part of our valuation. Zafgen's stated plan under this scenario is to preserve beloranib's premium pricing for the rare disease settings and develop a follow-on molecule for the large severe obesity indication. Given the impressive weight loss efficacy observed with beloranib and the fact that it comes without the need for concomitant diet and exercise, we believe that positive data in this Phase IIb trial could provide an additional $31/share to our estimates.

Downside scenario

The downside scenario of $20/share assumes the Phase III bestPWS 6-month data meeting only the reduction in body fat mass co-primary endpoint, but not the hyperphagia endpoint. While this result would probably still enable FDA approval for beloranib as a treatment of PWS, commercial uptake may be limited, as patients, physicians, and families all view hyperphagia as the key issue. By reducing beloranib penetrations to half of those in the base case scenario and lowering the probability of success to 40% in PWS and 33% in HIAO, we arrive at a valuation of beloranib sales in PWS of ~$9/share and in HIAO of ~$5/share.

Investment summary

A really impressive injectable drug for obesity… Beloranib acts via a novel mechanism of action to lead to rapid and impressive weight loss in the obese patients it has been tested on in early stage Phase I and II trials. Using a novel mechanism different from the ones used by other drugs currently on the market, this methionine aminopeptidase 2 (MetAP2) inhibitor leads to significant weight loss (up to 10% of body weight), in just 12 weeks.

…but it will not get to the market for obesity first: However, and despite the compound's impressive efficacy, the company has decided to try a different approach and not go with obesity as its lead indication for beloranib. If successful, this would possibly allow the drug to reach market faster, in addition to gaining other benefits along the way, including premium pricing.

Prader-Willi Syndrome: a rare, genetic, obesity-related disease. There are an estimated 21,000 PWS cases in the US, with 7,500 of them identified. PWS patients are characterized by hyperphagia, the inability to feel hunger, which leads them to overeat and (most) to become obese. After promising data from a 17-patient Phase II trial, Zafgen is testing the drug in the bestPWS Phase III trial, with data expected YE15. A second trial to be conducted in Europe is expected to start soon, and will be required for US and EU approval. Based on the efficacy observed thus far, we expect the drug to be approved. Zafgen plans to market beloranib on its own, via a specialty salesforce, and we project that it can become a significant product in PWS alone, reaching $750MM in peak US/EU 2029 sales.

HIAO doubles beloranib's commercial potential: Zafgen recently reported positive data from a 14-patient, Phase II trial of beloranib in patients with hypothalamic injury-associated obesity (HIAO). These patients develop obesity due to uncontrollable hunger, somewhat akin to an "acquired PWS", following surgery to remove craniopharyngiomas. Positive pivotal data in this setting would make HIAO the second rare disease indication for beloranib, doubling its market potential.

Potential catalysts: 1) Phase III beloranib PWS data (YE15), 2) IND application for ZGN-839 in NASH/T2DM (mid 15), 3) interim data from beloranib severe obesity trial (YE15)

Risks: 1) delays in EU PWS trial, 2) negative data in Phase III PWS trials, and 3) unanticipated safety signals of beloranib in ongoing trials. These risks, that if materialized, may result in significant volatility, and the fact that the majority of the value comes from a single product leads to the Speculative Risk qualifier on our rating.

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Key questions

		Our view
1.	**How do the changes in the Phase III bestPWS trial design affect its chances for success?**	**Although changes to trial design theoretically introduce new variables and risks, we believe that the specific changes improve the chances of success for the bestPWS Phase III trial**. The three major changes from Phase II to Phase III are: 1) patient population, 2) dose, and 3) primary endpoint selection. We believe the Phase III trial design builds on the strengths of and the lessons learned from the Phase II trial. The patient population now includes patients as young as 12, and limits the enrollment of patients living in group homes, where the restrictive environment may have potentially masked beloranib's benefits. Additionally, the higher 2.4 mg beloranib dose, to be used for the first time in PWS patients, had previously demonstrated strong weight-loss efficacy, albeit with more side effects, in obese patients. Finally, the new co-primary endpoints in the Phase III trial were the Phase II trial's secondary endpoints and were statistically significant.
2.	**How well the 2.4 mg dose fare in terms of tolerability?**	**Although the use of the 2.4 mg beloranib dose in the bestPWS trial is a potential risk, we believe the previously seen tolerability issues seen with this dose are less of an issue in PWS patients than they were in the general obese population**. The PWS KOLs we spoke with do not expect that the adverse events seen in general obese patients with the 2.4 mg dose, such as GI events and a slight delay falling asleep at night, to be an issue with PWS patients. They cite PWS patients' inherent disinclination to suffer GI events and that given that PWS patients have difficulty staying awake, a delay in falling asleep would be seen as a benefit.
3.	**What is the market opportunity in HIAO?**	**We view the market opportunity in HIAO as roughly equivalent to that in PWS. This would essential double the revenue that can be generated by beloranib**. Our estimates place the number of existing craniopharyngioma patients who develop obesity (HIAO patients) to around 3,000 and 5,000 in the US and EU, respectively. This is in comparison with nearly 3,700 and 6,000 addressable PWS patients in the US and EU that we believe beloranib can initially target. We project beloranib could bring in an additional ~$630MM in peak US/EU HIAO sales.
4.	**So, what is the plan for beloranib in general obesity?**	**Our understanding of management's current plan is that beloranib, if the Phase III program in PWS is successful, will be (p)reserved for the treatment of orphan diseases (like PWS and HIAO).** However, management remains interested in continuing to develop the drug in the general obese population. So, if the data continue to support the use of MetAP2 inhibitors in obesity (as in positive data from the Phase IIb ZAF-203 trial that will read out YE15), we expect ZFGN to use beloranib for rare diseases and develop its own proprietary MetAP2 inhibitor program for the treatment of weight management. Some of the advantages of this strategy include better economics to the future asset and the potential to adjust some of beloranib's properties, including avoiding penetration of the placenta and being brain impermeable—perhaps to offset any CNS and/or hypothalamus effects on sleep and/or circadian rhythms for the general population.

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Valuation

To value ZFGN shares, we use a sum-of-the-parts methodology, and estimate the probability adjusted NPV of the following: 1) beloranib sales in PWS and 2) the company's projected net cash position.

1) Beloranib sales in PWS ($30/share)

i) US sales

In our model, we assume that beloranib will be approved by the FDA for the treatment of PWS and launched in 2018. We anticipate Zafgen to promote beloranib without a partner by assembling a dedicated salesforce to target the handful of PWS excellence centers in the US.

ii) EU Sales

In our model, we assume that beloranib will receive EU marketing approval for treating PWS in 2019. We also assume that Zafgen will promote in the EU also without a partner.

US and EU beloranib sales

We model that beloranib could reach peak sales of $376MM and $395MM in the US and EU in 2031 and 2029, respectively, and a peak US/EU sales of $751MM in 2029 for the treatment of PWS patients.

Discount rate and probability of success (POS)

In calculating the net present value of beloranib's free cash flows, we use a 10% discount rate. We assign each territory a 60% POS that beloranib will be approved and achieves our projected level of sales in the US and EU market. Using these assumptions, we arrive at a probability-adjusted NPV for beloranib in PWS of $30/share.

Exhibit 2: Beloranib PWS NPV analysis ($MM) – US

($MM)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Total US Beloranib PWS Sales	0.0	0.0	0.0	89.5	157.0	211.4	285.9	293.9	302.1	310.5	319.2	328.1	337.2	346.6	356.2	366.2	376.4	38.7	19.9
Total US Beloranib PWS Revenue	**0.0**	**0.0**	**0.0**	**89.5**	**157.0**	**211.4**	**285.9**	**293.9**	**302.1**	**310.5**	**319.2**	**328.1**	**337.2**	**346.6**	**356.2**	**366.2**	**376.4**	**38.7**	**19.9**
Total Paid Royalties for US PWS Beloranib Sales	0.0	0.0	0.0	7.2	12.6	16.9	22.9	14.7	15.1	15.5	16.0	16.4	16.9	17.3	17.8	18.3	18.8	1.9	1.0
COGS	0.0	0.0	0.0	10.7	18.8	25.4	31.5	32.3	33.2	34.2	31.9	32.8	33.7	34.7	35.6	36.6	37.6	3.9	2.0
R&D	5.2	5.5	5.6	5.7	5.8	5.9	6.0	5.4	4.8	4.4	3.9	3.5	3.2	2.9	2.6	2.3	2.1	1.9	1.7
G&A	2.5	2.5	2.6	2.6	2.7	2.7	2.8	2.8	2.9	3.0	3.0	3.1	3.1	3.2	3.3	3.3	3.4	3.5	3.5
Sales expense	0.0	0.0	0.0	7.5	8.0	8.2	8.3	8.5	8.7	8.8	9.0	9.2	9.4	9.6	9.8	8.8	7.9	7.1	6.4
Marketing expense	0.0	0.0	0.0	2.0	2.5	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	1.5	1.5	1.5	1.5
Tax adjusted EBIT	(7.6)	(8.1)	(7.0)	45.7	88.5	101.6	137.5	147.7	152.3	157.1	164.0	169.0	174.1	179.4	184.7	192.0	198.3	15.1	3.0
Tax rate	*0%*	*0%*	*15%*	*15%*	*17%*	*32%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*20%*	*20%*
Beloranib sales free cash flow	**(7.6)**	**(8.1)**	**(7.0)**	**45.7**	**88.5**	**101.6**	**137.5**	**147.7**	**152.3**	**157.1**	**164.0**	**169.0**	**174.1**	**179.4**	**184.7**	**192.0**	**198.3**	**15.1**	**3.0**
Discount period	*0.94*	*1.94*	*2.94*	*3.94*	*4.94*	*5.94*	*6.94*	*7.94*	*8.94*	*9.94*	*10.94*	*11.94*	*12.94*	*13.94*	*14.94*	*15.94*	*16.94*	*17.94*	*18.94*
Discount factor	*0.91*	*0.83*	*0.76*	*0.69*	*0.62*	*0.57*	*0.52*	*0.47*	*0.43*	*0.39*	*0.35*	*0.32*	*0.29*	*0.26*	*0.24*	*0.22*	*0.20*	*0.18*	*0.16*
PV of Beloranib free cash flow	**(7.0)**	**(6.7)**	**(5.3)**	**31.4**	**55.3**	**57.7**	**71.0**	**69.3**	**65.0**	**60.9**	**57.8**	**54.2**	**50.7**	**47.5**	**44.5**	**42.0**	**39.5**	**2.7**	**0.5**

Discount Rate	10%
Perpetual Growth Rate	0%
Final year FCF	$0
Terminal Value	$0
Discount Factor	0.18
Present Value of Terminal Value	**$0**
Present Value of Cash Flows	**$731**
Present Value of Total Cash Flows	**$731**
Fully Dilutued Shares Outstanding (MM)	27.8
NPV of US beloranib free cash flow	**$26.28**
Probability of success	***60%***
NPV of beloranib free cash flows (probability-adjusted)	**$15.77**

Source: RBC Capital Markets estimates

Exhibit 3: Beloranib PWS NPV analysis ($MM) – EU

($MM)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Total EU Beloranib PWS Sales	0.0	0.0	0.0	0.0	88.7	174.9	251.6	338.4	345.9	353.6	361.5	369.5	377.7	386.1	394.7	40.4	20.6	21.1	21.6
Total EU Beloranib PWS Revenue	**0.0**	**0.0**	**0.0**	**0.0**	**88.7**	**174.9**	**251.6**	**338.4**	**345.9**	**353.6**	**361.5**	**369.5**	**377.7**	**386.1**	**394.7**	**40.4**	**20.6**	**21.1**	**21.6**
Total Paid Royalties for EU Beloranib Sales	0.0	0.0	0.0	0.0	7.1	14.0	20.1	16.9	17.3	17.7	18.1	18.5	18.9	19.3	19.7	2.0	1.0	1.1	1.1
COGS	0.0	0.0	0.0	0.0	10.6	21.0	27.7	37.2	38.1	38.9	36.1	37.0	37.8	38.6	39.5	4.0	2.1	2.1	2.2
R&D	5.2	5.5	5.6	5.7	5.8	5.9	6.0	5.4	4.8	4.4	3.9	3.5	3.2	2.9	2.6	2.3	2.1	1.9	1.7
G&A	2.5	2.5	2.6	2.6	2.7	2.7	2.8	2.8	2.9	3.0	3.0	3.1	3.1	3.2	3.3	3.3	3.4	3.5	3.5
Sales expense	0.0	0.0	0.0	2.5	4.0	4.1	4.2	4.2	4.3	4.4	4.5	4.6	4.7	4.2	3.8	3.4	3.1	2.8	2.5
Marketing expense	0.0	0.0	0.0	1.5	2.0	2.0	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	1.0	1.0	1.0	1.0
Tax adjusted EBIT	(7.6)	(8.1)	(7.0)	(10.5)	46.9	85.1	122.4	175.0	179.4	183.8	190.6	195.2	199.9	205.0	210.2	15.8	5.2	7.0	7.7
Tax rate	*0%*	*0%*	*15%*	*15%*	*17%*	*32%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*20%*	*20%*
Beloranib sales free cash flow	**(7.6)**	**(8.1)**	**(7.0)**	**(10.5)**	**46.9**	**85.1**	**122.4**	**175.0**	**179.4**	**183.8**	**190.6**	**195.2**	**199.9**	**205.0**	**210.2**	**15.8**	**5.2**	**7.0**	**7.7**
Discount period	*0.94*	*1.94*	*2.94*	*3.94*	*4.94*	*5.94*	*6.94*	*7.94*	*8.94*	*9.94*	*10.94*	*11.94*	*12.94*	*13.94*	*14.94*	*15.94*	*16.94*	*17.94*	*18.94*
Discount factor	*0.91*	*0.83*	*0.76*	*0.69*	*0.62*	*0.57*	*0.52*	*0.47*	*0.43*	*0.39*	*0.35*	*0.32*	*0.29*	*0.26*	*0.24*	*0.22*	*0.20*	*0.18*	*0.16*
PV of Beloranib free cash flow	**(7.0)**	**(6.7)**	**(5.3)**	**(7.2)**	**29.3**	**48.3**	**63.2**	**82.1**	**76.5**	**71.3**	**67.2**	**62.6**	**58.2**	**54.3**	**50.6**	**3.4**	**1.0**	**1.3**	**1.3**

Discount Rate	10%
Perpetual Growth Rate	0%
Final year FCF	$0
Terminal Value	$0
Discount Factor	0.18
Present Value of Terminal Value	**$0**
Present Value of Cash Flows	**$645**
Present Value of Total Cash Flows	**$645**
Fully Dilutued Shares Outstanding (MM)	27.8
NPV of beloranib free cash flow	**$23.17**
Probability of success	***60%***
NPV of beloranib free cash flows (probability-adjusted)	**$13.90**

Source: RBC Capital Markets estimates

2) Beloranib sales in HIAO ($17/share)

i) US sales

In our model, we assume that beloranib will be approved by the FDA for the treatment of HIAO and launched in 2019. We anticipate Zafgen to promote beloranib without a partner.

ii) EU Sales

In our model, we assume that beloranib will receive EU marketing approval for treating HIAO in 2020. We also assume that Zafgen will promote in the EU also without a partner.

US and EU beloranib sales

We model that beloranib could reach peak sales of $323MM and $331MM in the US and EU in 2031 and 2028, respectively, and a peak US/EU sales of $628MM in 2028 for the treatment of HIAO patients.

Discount rate and probability of success (POS)

In calculating the net present value of beloranib's free cash flows, we use a 10% discount rate. We assign each territory a 50% POS that beloranib will be approved and achieves our projected level of sales in the US and EU markets. Using these assumptions, we arrive at a probability-adjusted NPV for beloranib in HIAO of $17/share.

Exhibit 4: Beloranib HIAO NPV analysis ($MM) – US

($MM)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Total US Beloranib HIAO Sales	0.0	0.0	0.0	0.0	74.2	128.8	186.3	251.9	258.9	266.2	273.6	281.2	289.0	297.1	305.3	313.9	322.6	33.2	17.0
Total US Beloranib HIAO Revenue	**0.0**	**0.0**	**0.0**	**0.0**	**74.2**	**128.8**	**186.3**	**251.9**	**258.9**	**266.2**	**273.6**	**281.2**	**289.0**	**297.1**	**305.3**	**313.9**	**322.6**	**33.2**	**17.0**
Total Paid Royalties for US Beloranib Sales	0.0	0.0	0.0	0.0	5.9	10.3	14.9	12.6	12.9	13.3	13.7	14.1	14.5	14.9	15.3	15.7	16.1	1.7	0.9
COGS	0.0	0.0	0.0	0.0	8.9	15.5	20.5	27.7	28.5	29.3	27.4	28.1	28.9	29.7	30.5	31.4	32.3	3.3	1.7
R&D	5.2	5.5	5.6	5.7	5.8	5.9	6.0	5.4	4.8	4.4	3.9	3.5	3.2	2.9	2.6	2.3	2.1	1.9	1.7
G&A	2.5	2.5	2.6	2.6	2.7	2.7	2.8	2.8	2.9	3.0	3.0	3.1	3.1	3.2	3.3	3.3	3.4	3.5	3.5
Sales expense	0.0	0.0	0.0	7.5	8.0	8.2	8.3	8.5	8.7	8.8	9.0	9.2	9.4	9.6	9.8	8.8	7.9	7.1	6.4
Marketing expense	0.0	0.0	0.0	2.0	2.5	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	3.0	1.5	1.5	1.5	1.5
Tax adjusted EBIT	(7.6)	(8.1)	(7.0)	(15.1)	33.5	56.6	85.0	124.7	128.8	132.9	138.8	143.1	147.5	152.0	156.6	163.1	168.6	11.4	1.1
Tax rate	*0%*	*0%*	*15%*	*15%*	*17%*	*32%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*20%*	*20%*
Beloranib sales free cash flow	**(7.6)**	**(8.1)**	**(7.0)**	**(15.1)**	**33.5**	**56.6**	**85.0**	**124.7**	**128.8**	**132.9**	**138.8**	**143.1**	**147.5**	**152.0**	**156.6**	**163.1**	**168.6**	**11.4**	**1.1**
Discount period	*0.94*	*1.94*	*2.94*	*3.94*	*4.94*	*5.94*	*6.94*	*7.94*	*8.94*	*9.94*	*10.94*	*11.94*	*12.94*	*13.94*	*14.94*	*15.94*	*16.94*	*17.94*	*18.94*
Discount factor	*0.91*	*0.83*	*0.76*	*0.69*	*0.62*	*0.57*	*0.52*	*0.47*	*0.43*	*0.39*	*0.35*	*0.32*	*0.29*	*0.26*	*0.24*	*0.22*	*0.20*	*0.18*	*0.16*
PV of Beloranib free cash flow	**(7.0)**	**(6.7)**	**(5.3)**	**(10.4)**	**20.9**	**32.1**	**43.9**	**58.5**	**54.9**	**51.5**	**48.9**	**45.9**	**43.0**	**40.3**	**37.7**	**35.7**	**33.5**	**2.1**	**0.2**

Discount Rate	10%
Perpetual Growth Rate	0%
Final year FCF	$0
Terminal Value	$0
Discount Factor	0.18
Present Value of Terminal Value	**$0**
Present Value of Cash Flows	**$520**
Present Value of Total Cash Flows	**$520**
Fully Dilutued Shares Outstanding (MM)	27.8
NPV of US beloranib free cash flow	**$18.69**
Probability of success	***50%***
NPV of beloranib free cash flows (probability-adjusted)	**$9.34**

Source: RBC Capital Markets estimates

Exhibit 5: Beloranib HIAO NPV analysis ($MM) – EU

($MM)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
Total EU Beloranib HIAO Sales	0.0	0.0	0.0	0.0	0.0	66.6	130.5	197.2	296.5	303.1	309.8	316.7	323.8	331.0	236.8	34.6	17.7	18.1	18.5
Total EU Beloranib Revenue	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**66.6**	**130.5**	**197.2**	**296.5**	**303.1**	**309.8**	**316.7**	**323.8**	**331.0**	**236.8**	**34.6**	**17.7**	**18.1**	**18.5**
Total Paid Royalties for EU Beloranib Sales	0.0	0.0	0.0	0.0	0.0	5.3	10.4	9.9	14.8	15.2	15.5	15.8	16.2	16.5	11.8	1.7	0.9	0.9	0.9
COGS	0.0	0.0	0.0	0.0	0.0	8.0	14.4	21.7	32.6	33.3	31.0	31.7	32.4	33.1	23.7	3.5	1.8	1.8	1.8
R&D	5.2	5.5	5.6	5.7	5.8	5.9	6.0	5.4	4.8	4.4	3.9	3.5	3.2	2.9	2.6	2.3	2.1	1.9	1.7
G&A	2.5	2.5	2.6	2.6	2.7	2.7	2.8	2.8	2.9	3.0	3.0	3.1	3.1	3.2	3.3	3.3	3.4	3.5	3.5
Sales expense	0.0	0.0	0.0	2.5	4.0	4.1	4.2	4.2	4.3	4.4	4.5	4.6	4.7	4.2	3.8	3.4	3.1	2.8	2.5
Marketing expense	0.0	0.0	0.0	1.5	2.0	2.0	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	1.0	1.0	1.0	1.0
Tax adjusted EBIT	(7.6)	(8.1)	(7.0)	(10.5)	(12.0)	26.3	58.7	98.0	152.4	156.2	162.1	166.1	170.1	174.6	123.0	12.6	3.6	5.0	5.6
Tax rate	*0%*	*0%*	*15%*	*15%*	*17%*	*32%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*20%*	*20%*
Beloranib sales free cash flow	**(7.6)**	**(8.1)**	**(7.0)**	**(10.5)**	**(12.0)**	**26.3**	**58.7**	**98.0**	**152.4**	**156.2**	**162.1**	**166.1**	**170.1**	**174.6**	**123.0**	**12.6**	**3.6**	**5.0**	**5.6**
Discount period	*0.94*	*1.94*	*2.94*	*3.94*	*4.94*	*5.94*	*6.94*	*7.94*	*8.94*	*9.94*	*10.94*	*11.94*	*12.94*	*13.94*	*14.94*	*15.94*	*16.94*	*17.94*	*18.94*
Discount factor	*0.91*	*0.83*	*0.76*	*0.69*	*0.62*	*0.57*	*0.52*	*0.47*	*0.43*	*0.39*	*0.35*	*0.32*	*0.29*	*0.26*	*0.24*	*0.22*	*0.20*	*0.18*	*0.16*
PV of Beloranib free cash flow	**(7.0)**	**(6.7)**	**(5.3)**	**(7.2)**	**(7.5)**	**14.9**	**30.3**	**46.0**	**65.0**	**60.6**	**57.1**	**53.2**	**49.6**	**46.2**	**29.6**	**2.8**	**0.7**	**0.9**	**0.9**

Discount Rate	10%
Perpetual Growth Rate	0%
Final year FCF	$0
Terminal Value	$0
Discount Factor	0.18
Present Value of Terminal Value	**$0**
Present Value of Cash Flows	**$424**
Present Value of Total Cash Flows	**$424**
Fully Dilutued Shares Outstanding (MM)	27.8
NPV of beloranib free cash flow	**$15.25**
Probability of success	***50%***
NPV of beloranib free cash flows (probability-adjusted)	**$7.62**

Source: RBC Capital Markets estimates

3) Zafgen's projected net cash position ($6/share)

Zafgen ended 3Q14 with $127.0MM in cash and $7.5MM in debt. Zafgen intends to raise an additional $100-$120MM in a capital raise in January 2015 to strengthen its cash position. In making our 12-month price target, we will consider projected net cash in 12 months. By adding new capital, estimated FY2015 net income, subtracting any FY2015 amortized revenue, and adding back FY2015 non-cash stock-based compensation, we project Zafgen to end FY2015 with around $187MM in net cash.

Exhibit 6: ZFGN sum-of-the-parts value

ZFGN NPV (probability-adjusted)	
Beloranib PWS NPV - US	$15.77
Beloranib PWS NPV - EU	$13.90
Beloranib HIAO NPV - US	$9.34
Beloranib HIAO NPV - EU	$7.62
Projected Net Cash	$6.46
Sum-of-the-parts value for ZFGN	**$53.09**

Source: RBC Capital Markets estimates

Price target impediments

As the majority of Zafgen's value lies with the beloranib asset, and particularly in the rare disease indications, any further delays to the filing timeline for the beloranib would negatively affect our valuation. Other factors that can negatively influence our valuation include increased competition, regulatory setbacks, and lower than projected penetrations for beloranib. Factors that can positively affect our valuation include more favorable pricing, positive data from other early-stage Zafgen programs (such as ZGN-839 or a new compound for general obese individuals), and M&A, which we have not included in our valuation.

Company Overview

Zafgen is a clinical-stage biotechnology company developing MetAP2 inhibitors for the treatment of individuals with obesity. The company went public by issuing a $110MM IPO in June 2014 to fund its ongoing clinical trials for its lead compound beloranib, a first-in-class MetAP2 inhibitor. Beloranib is currently in clinical trials to treat patients with Prader-Willi Syndrome (PWS), hypothalamic injury (HIAO), and general obesity. Zafgen's pipeline also includes an oral MetAP2 inhibitor, ZGN-839, in preclinical studies for the treatment of nonalcoholic steatohepatitis (NASH) and type 2 diabetes. Founded in 2005, Zafgen is based in Cambridge, MA and currently has 18 full-time employees.

Exhibit 7: ZFGN's pipeline

Drug (Target)	Trial	Indication	Stage
beloranib (MetAP2 inhibitor)	bestPWS	Prader-Willi Syndrome (PWS)	Phase III
	ZAF-221	hypothalamic injury-associated obesity (HIAO)	Phase II
	ZAF-203	severe obesity	Phase II
ZGN-839 (oral MetAP2 inhibitor)		nonalcoholic steatohepatitis (NASH)/ type 2 diabetes mellitus (T2DM)	Preclinical

Source: Company reports

Exhibit 8: Expected newsflow

Event	Indication	Timing
Submit IND for oral ZGN-839 program	NASH/T2DM	mid 2015
Initiate second PWS trial (ZAF-312) in EU	PWS	mid 2015
6 month Ph III bestPWS readout	PWS	YE15
Interim Ph II ZAF-203 data	severe obesity	YE15
NDA submission for beloranib in PWS	PWS	2016
12 month data from ZAF-312 PWS trial	PWS	YE16

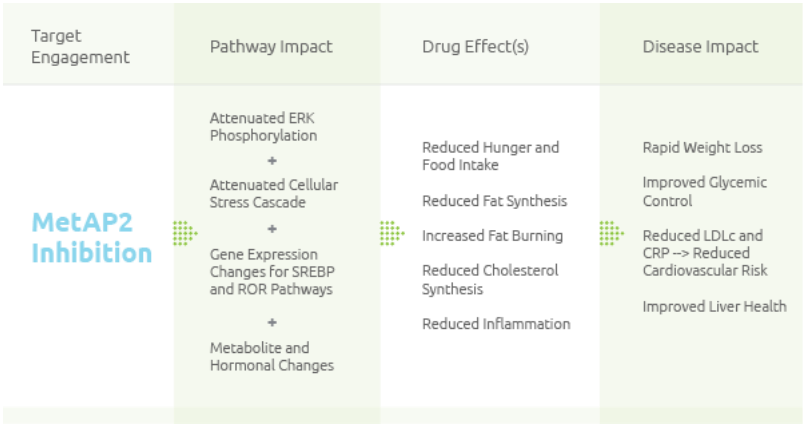
Source: Company reports, RBC Capital Markets estimates

Beloranib: inhibiting MetAP2 to treat obesity

Repurposed from being an angiogenesis inhibitor, beloranib has shown impressive weight loss efficacy. Zafgen is developing beloranib as a twice-weekly, subcutaneous injection to treat obesity due to PWS and hypothalamic injury (i.e., craniopharyngioma or HIAO) and also for the treatment of general obesity. Beloranib is a synthetic derivative of the natural compound fumagillin, an antimicrobial agent isolated from *Aspergillus fumigatus*. In humans, fumagillin and its derivatives possess anti-angiogenesis properties and were previously developed for the treatment of cancer. These compounds bind the MetAP2 protein (methionine aminopeptidase 2), an enzyme that removes the initial methionine residue in a nascent peptide chain.

Beloranib was similarly tested for oncology indications but instead showed more remarkable effects in inducing significant and sustained weight reduction. The complex physiology behind obesity masks the precise anti-obesity effect of MetAP2 inhibitors, which currently proposes a link between MetAP2 inhibition and stimulation of fat metabolism and suppression of hunger and food intake, as shown in the exhibit below. More scientific studies on pathways leading to obesity are still needed to further elucidate beloranib's mechanism of action.

Exhibit 9: Anti-obesity mechanism of action for MetAP2 inhibitors



Source: Company reports

Beloranib is currently focused on rare diseases versus obesity

Unlike other therapeutic agents within the weight management and obesity space, Zafgen will seek regulatory approval for beloranib through orphan disease indications. The company cites the immense scale and costs of clinical trials focusing directly on the general obese population as factors to pursue alternative strategies. Additionally, other obesity drugs mostly target the CNS and the hypothalamus, in particular, to reduce cravings and the sensation of hunger. Beloranib differentiates itself from these drugs through its novel mechanism of action through MetAP2 inhibition and stimulation of fat metabolism.

Taken together, Zafgen is initially introducing beloranib as a treatment to reduce weight and hyperphagia (increased appetite) in a couple of rare indications in addition to severe obesity in the general population. Most advanced in clinical development is the treatment of obese subjects with PWS, for which beloranib was granted orphan drug designation by the FDA and EU in January 2013 and June 2014, respectively. Beloranib is also in clinical trials for the treatment of patients with hypothalamic injury-associated obesity (HIAO), commonly from the treatment of a rare brain tumor craniopharyngioma. Regulatory approval in either of

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these two indications would result in faster market access for beloranib than the more commonly treaded approach through the general obese population.

To date, beloranib has completed testing in five clinical trials spanning generally obese and obese patients with PWS. Initial protocols focused on intravenous administrations of beloranib before settling on a twice weekly, subcutaneous regimen at a dose of around 1-2 mg. The aggregate weight loss data point to significant placebo-adjusted weight reductions. Moreover, indicators for sense of hunger are markedly reduced, and decreases in cardiovascular markers are also associated with beloranib use. The general safety data indicate mild to moderate side effects related to sleep disturbances and general gastrointestinal adverse events.

An introduction to Prader-Willi syndrome

An unusual disease marked by unusual genetics

Prader-Willi syndrome (PWS) is a behavioral and metabolic syndrome that is the most common genetic cause for life-threatening childhood obesity. Estimates for PWS prevalence range from 1 in 10,000 to 1 in 30,000 individuals, with a consensus around 1 in 15,000. The syndrome results from specific loss of paternal genes, typically due to deletions, at the PWS genetic region on chromosome 15q11-13. The maternal contribution is not sufficient as the maternal alleles undergo a genetic phenomenon, termed imprinting, where the alleles on the maternal chromosome 15q11-13 are methylated and silenced. More than one gene is involved in PWS, as this locus consists of five protein-encoding genes and six snoRNA genes. Around 70% of PWS individuals inherit a paternal chromosome 15 with deletions at the 15q11-13 locus. Another 25-30% of cases arise from uniparental disomy where individuals inherit two copies of the maternal chromosome 15 and none from the father, thus lacking paternal gene expression as both maternal chromosome 15s are imprinted at the PWS locus. Less than 3% of PWS cases arise due to other less common genetic mutations, such as imprinting defects on the paternal chromosome 15.

Regardless of the genetic origin, the clinical manifestations of PWS remain the same, and the disease typically progresses in five phases, as shown in the following exhibit. A Phase 0 occurs in utero, with reported fewer fetal movements and lower birth weight and length in newborns. In the first phase, newborns are hypotonic (low muscle tone) and are actually underweight due to poor suck from weakened muscles. In the second phase from age's two to eight, the child's weight increases above the normal weight, and the abnormal increase in appetite may lead to overweight or obesity if the diet is not carefully monitored. The third phase starts at a median age of eight-years old and lasts into adulthood. This phase is marked by hyperphagia (insatiable appetite) and rarely feeling full. Anecdotes from parents of PWS patients suggest that there is an instantaneous and irreversible onset of hyperphagia. However, a small minority of individuals (estimated <10%) may progress into the fourth phase later in life where an individual previously in phase three no longer has hyperphagia and is able to feel full.

Exhibit 10: PWS progresses in five phases

Phase	Age (yrs)	Characteristics
0	in utero	Decreased birth weight, length, and fetal movements
1	0 - 2.1	Hypotonic (low muscle tone) and underweight
2	2.1 - 8	Increase in appetite with overweight or obesity
3	8 - adulthood	Hyperphagia (insatiable appetite) and rarely feel full
4	adulthood	A small portion of patients able to feel full

Source: S. B. Cassidy et al., Genetics in Medicine, Vol. 14(1), p10–26, 2012; RBC Capital Markets

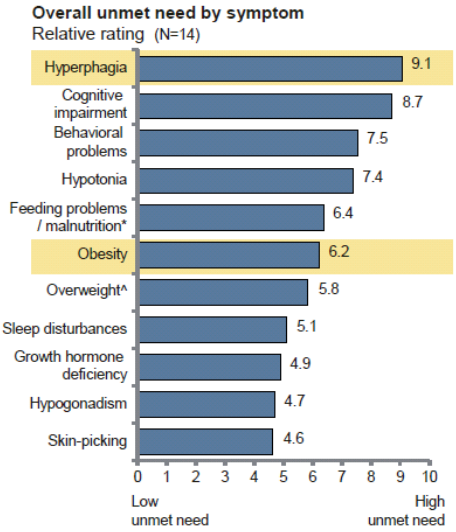
Our KOLs have indicated that the average age of diagnosis was around 8 years old in 2000, but due to increased awareness and PWS as a differential diagnosis for infant hypotonia, PWS individuals are now commonly diagnosed around two months of age. Genetic tests, such as methylation and deletion tests, can be then used to confirm the genetic roots of the disorder.

Symptoms of PWS: hyperphagia and obesity are key morbidities

PWS individuals exhibit a host of symptoms and morbidities, including infantile hypotonia, developmental disability, hyperphagia leading to obesity, behavioral and psychiatric disturbances, hypogonadism, short stature and growth hormone deficiency, and sleep abnormalities (e.g., narcolepsy). Other medical issues involve high pain threshold, lack of vomiting, and skin lesions and bruises from apparently common skin picking habits of PWS individuals. In children, the most frequent causes of death are respiratory, febrile illnesses, and choking; while, obesity-related cardiovascular problems, gastric causes, and sleep apneas are the most frequent causes in adults.

As shown in the following exhibit, while PWS patients have a large number of symptoms, hyperphagia and obesity are two symptoms that represent significant, unmet needs and can be potentially targeted by a drug. Other symptoms, such as growth hormone deficiency and hypotonia, can be managed by growth hormone therapy, though the route of administration and costs can be challenging. As for symptoms like cognitive impairment and behavioral problems, there are no therapeutic agents that treat those symptoms in PWS patients, although SSRIs (selective serotonin reuptake inhibitors) have been reported in reducing skin picking, compulsivity, and aggressive episodes in some PWS individuals. Additionally, psychological and behavioral therapies are also suggested for better control.

Exhibit 11: Hyperphagia and obesity both have large unmet needs



Source: Company reports

Growth hormone therapy in PWS

There is no cure for PWS, and current treatments are only symptomatic. In the absence of the now standard of care, growth hormone (GH) replacement, the average height is 155 cm for males and 148 cm for females. GH therapy has been an important treatment option to stimulate growth in children with PWS. The major physical improvements after GH treatment include the following: increased height and growth rate, increased hand and/or foot size, increase in muscle development, and decrease in body mass index (BMI). However, intelligence quotient (IQ), appetite, and behavior problems of treated PWS patients are seldom changed.

In June 2000, the FDA approved the use of Genotropin (Pharmacia, acquired by Pfizer) for the treatment of growth failure due to PWS. In April 2010, the FDA approved the second growth hormone, Omnitrope (Sandoz), to be used in children with PWS. Although consensus has been established that GH is beneficial for children with PWS, there is no specific guideline to suggest the best age to start or stop GH therapy. A recent study showed that GH therapy could bring benefits to infants with PWS as early as two to three months of age. A child with PWS can be assessed for GH treatment at any age, and earlier treatment seems to provide the best opportunity to have treatment effects in stature, body composition, and motor functions. A recent study published in 2013 followed 60 prepubertal children who had eight years of continuous GH treatment, and concluded that GH treatment could be an effective way to prevent obesity in children with PWS.

Controlling hyperphagia and obesity in PWS

Many families employ strategies to control hyperphagia and obesity for PWS patients, as drugs for weight management (i.e., Vivus' Qsymia) have not worked. In these patients, occurrences such as food-seeking behavior, hoarding or foraging for food, eating of inedibles, and stealing of food or money to buy food are commonplace. These behaviors are compounded by a decreased caloric requirement from slower metabolism (decreased activity and decreased lean muscle mass) compared with normal individuals. Therefore, many families resort to implementing mechanisms (such as placing locks on kitchen cabinets and refrigerators to limit food access, strict diets, and enforced physical activity) to limit access to food and control obesity onset.

Alternatively, an estimated 15-20% of PWS individuals become institutionalized and live in group-home settings. In group homes specific to PWS individuals, the environment is more structured and restricted than it is in their own family homes. Weight control remains one of the top priorities of such community living. Exercise is promoted, and the individuals' caloric intake is heavily monitored with diets typically in the 1,000-1,800 calories range (much lower than typical for a normal individual). With such carefully planned and controlled supervision in either family or group homes, individuals who successfully maintain their weight can live a normal lifespan. The average life expectancy of PWS individuals is estimated to be around 32 years old, but some individuals in group homes have been reported to live past 50 years of age.

A review of beloranib's clinical program in PWS

1) Phase II ZAF-211 in obese PWS patients

- *Study started June 2013*
- *Study completed November 2013*

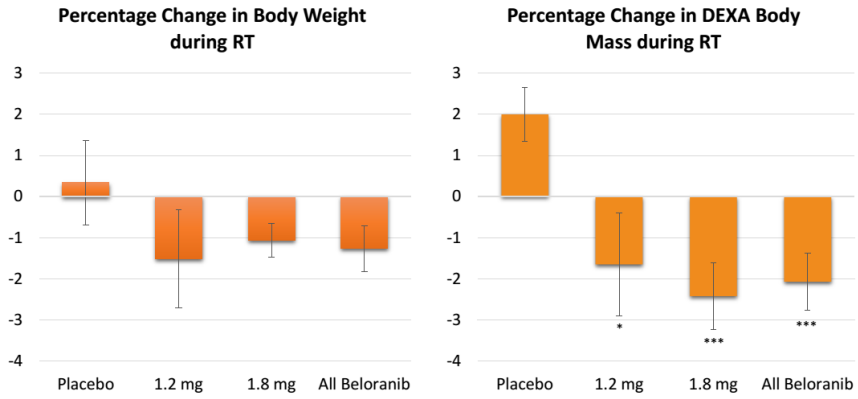
Study design: The randomized, double-blind, placebo-controlled, Phase II, ZAF-211 trial enrolled 17 obese patients with PWS who lived in group homes near the University of Florida's Gainesville campus. Enrolled patients underwent a two-week placebo run-in period to acclimate patients to the trial's procedures. Patients were then randomized 2:1 to receive twice-weekly, subcutaneous beloranib (n=11) or placebo (n=6). Patients on beloranib received either 1.2 mg (n=5) or 1.8 mg (n=6) as their doses for four weeks. At the end of four weeks, all patients were given the option of receiving four additional weeks of open-label 1.8 mg beloranib treatment.

Patient population: The 17 enrolled patients lived in a group-home setting where caretakers carefully monitored their access to food and placed subjects on a restricted diet. In such group-home settings, PWS subjects have limited caloric intake around an average of 1,200-1,300 calories per day, well below normal dietary recommendations (average daily intake of 2,000-2,500 calories). Food allowances were actually increased by 50% in the study in order to highlight the effects of treatment on body weight gain. The patients had an average age of 33.9 years old, and the BMI requirements (≥25 kg/m^2) were lower than those of other beloranib studies. The final patient population had an average BMI of 31.4 kg/m^2 (range 26-44). The average excess body weight was 14.6 kg with a range of 1.8-43.3 kg.

Endpoints: The primary endpoint of the study was percent change in body weight after four weeks on drug. The secondary endpoints further looked at absolute change in body weight (in kg) and change in hyperphagia behavior as assessed by the Dykens questionnaire given to the caretakers.

Weight loss efficacy: PWS subjects only showed modest percentage decreases in body weight during the four-week randomized treatment. Both doses of beloranib yielded around 1% decrease in body weight that was not statistically significant as compared to placebo. However, other metrics for body composition fared better in the analysis: percentage decrease in body mass as measured by DEXA (dual-energy X-ray absorptiometry) was around 2% and statistically significant for both doses.

Exhibit 12: Modest weight loss seen in PWS subjects



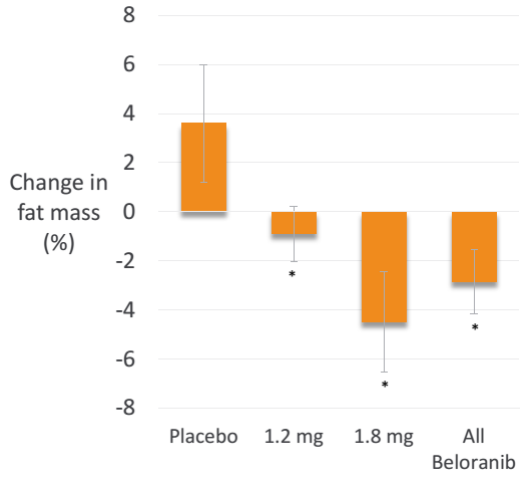
p values (by ANCOVA): *, p<0.05; **, p<0.01; ***, p<0.005

Source: Company reports

Treatment with beloranib resulted in a statistically significant decrease in fat mass. This endpoint will be used as a registration endpoint in the ongoing Phase III trial.

In contrast to changes in body weight, change in fat mass demonstrated a more impressive outcome with beloranib treatment. DEXA revealed a statistically significant decrease in fat mass at both doses, with around 4% decrease at 1.8 mg, while placebo patients had a nearly 4% increase in fat mass. Given this statistically significant 8% difference, demonstrated in just four weeks of treatment, the company has decided to use this metric as a co-primary endpoint in the subsequent Phase III trial for beloranib in PWS patients.

Exhibit 13: Beloranib treatment led to a statistically significant decrease in fat mass



p-values (by ANCOVA): *p<0.05
Source: Company reports

Hyperphagia test: The Dykens Hyperphagia-related Behavior Score measures responses taken by patients' caretakers and yields a total score based on a scale of 0-4 for severity and frequency in a number of behavior-related metrics due to hyperphagia. The test is further divided into three sub-scores of behavior (capacities of individuals to engage in a wider array of food-seeking behaviors), drive (drive for food), and severity (non-food maladaptive and compulsive behaviors).

Exhibit 14: Sample Dykens Hyperphagia questionnaire

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 appear?
	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?

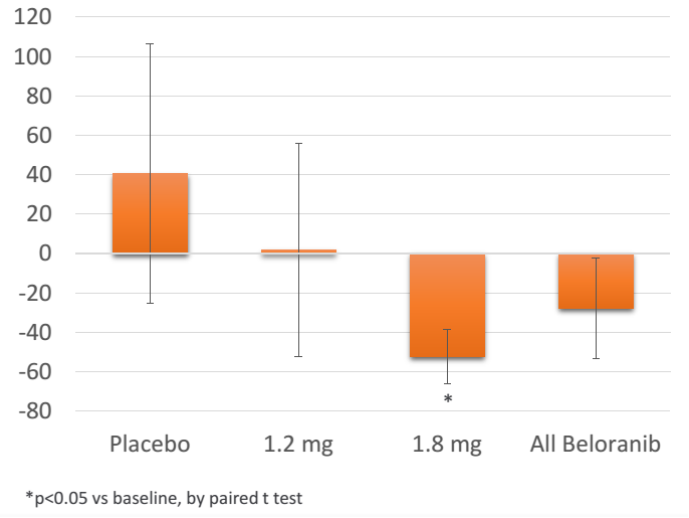
**This question has been removed from the questionaire for the Phase III bestPWS trial

Source: Company reports, RBC Capital Markets

The trial measured the percentage change from baseline for the total score for each individual patient. The Dykens questionnaire is usually given to caretakers, as patients' own responses tend to become unreliable over time as they realize which types of answers are preferred on the test. However, other confounders can still come into play. In the group-home setting, multiple shifts of caretakers may look over each patient, thus the caretaker who responds to the Dykens may not be aware of activity occurring outside of his or her personal time with the patient. This frequent turnover may introduce high variability, as the subjective nature of the questions asks for the frequency in behaviors regarding each patient. Nevertheless, based on the total score, there was a statistically significant, 56% decrease from baseline in the 1.8 mg beloranib-treated cohort, while the placebo-treated cohort's scores increased by 40%.

Treatment with beloranib resulted in significant decreases in hyperphagia, as measured by the Dykens questionnaire. This metric will also be used as one of the registration endpoints.

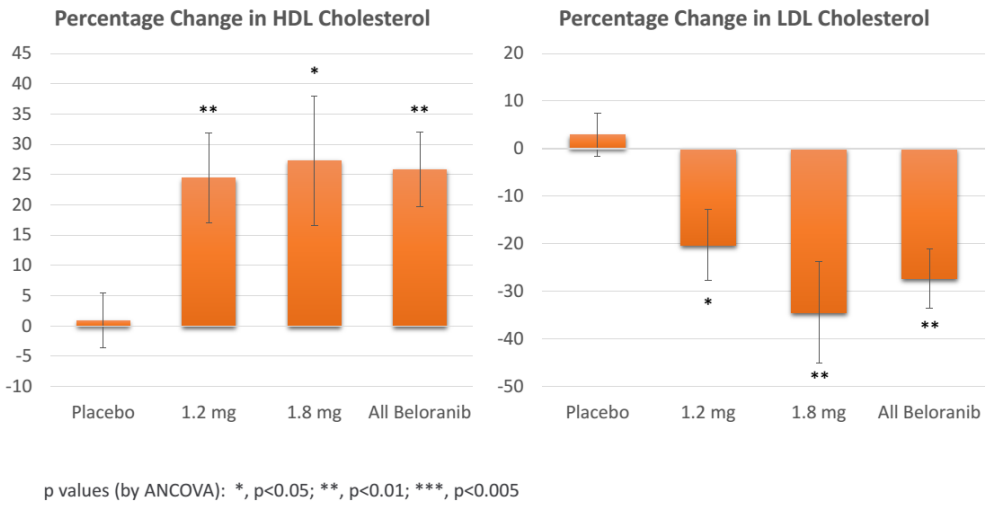
Exhibit 15: 1.8 mg beloranib demonstrated significant decrease in the Dykens score



Source: Company reports

Other results: Cardiovascular biomarkers showed improvement with beloranib treatment and included ~25% increases in high-density lipoprotein (HDL) cholesterol and ~20-30% decrease in low-density lipoprotein (LDL) cholesterol across the two doses, both statistically significant.

Exhibit 16: Percentage changes in cardiovascular biomarkers



Source: Company reports

Safety: Generally, beloranib was well tolerated in the PWS patient population and perhaps even better tolerated in comparison to beloranib in the previously studied general obese individuals. In 11 patients taking beloranib, nine reported a treatment-emergent adverse event (TEAE) for a total of 24 events (four relating to injection site reactions). In the placebo group, 6/6 patients reported a TEAE, for 17 total events (two relating to injection site reactions). Injection-site bruising was the most common side effect across treatment and placebo groups. Of potential concern, there was one reported event of psychotic disorder in one patient receiving 1.2 mg of beloranib. As opposed to what were witnessed in general obese patients, PWS subjects did not experience disturbances to sleeping patterns. The sleep quality total score in beloranib-treated patients was well below the threshold for poor sleep quality, and subjects did not experience an increase in sleep latency.

Exhibit 17: Treatment-emergent adverse events in the ZAF-211 trial

	Beloranib 1.2 mg (n=5)	Beloranib 1.8 mg (n=6)	Beloranib Combined (n=11)	Placebo (n=6)
	Subjects/Events	Subjects/Events	Subjects/Events	Subjects/Events
Any TEAE	5 (100%)/ 12	4 (66.7%)/ 12	9 (81.8%)/ 24	6 (100%)/ 17
Injection site bruising	2 (40.0%)/ 3	1 (16.7%)/ 1	3 (27.3%)/ 4	2 (33.3%)/ 2
Abdominal pain	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	0 / 0
Musculoskeletal pain	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Contusions	0 / 0	1 (16.7%)/ 2	1 (9.1%)/ 2	0 / 0
Pruritus	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	0 / 0
Injection site pain	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Injectino site pruritis	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Injection site rash	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Injection site swelling	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Insomnia	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Nightmare	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Mood altered	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	0 / 0
Decreased appetite	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	1 (16.7%)/ 2
Psychotic disorder	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	0 / 0
Thrombocytopenia	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Adrenal insufficiency	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	0 / 0
Blood serum decreased	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	2 (33.3%)/ 2
N-telopeptide urine increased	1 (20.0%)/ 1	0 / 0	1 (9.1%)/ 1	0 / 0
Hyperhidrosis	0 / 0	1 (16.7%)/ 1	1 (9.1%)/ 1	0 / 0
Non-cardiac chest pain	0 / 0	0 / 0	0 / 0	1 (16.7%)/ 1
Palpitations	0 / 0	0 / 0	0 / 0	1 (16.7%)/ 1
Hypoglycemia	0 / 0	0 / 0	0 / 0	2 (33.3%)/ 2
Fatigue	0 / 0	0 / 0	0 / 0	1 (16.7%)/ 1
Headache	0 / 0	0 / 0	0 / 0	1 (16.7%)/ 3
Cough	0 / 0	0 / 0	0 / 0	1 (16.7%)/ 1
Respiratory tract congestion	0 / 0	0 / 0	0 / 0	1 (16.7%)/ 1
Photophobia	0 / 0	0 / 0	0 / 0	1 (16.7%)/ 1

Source: Company reports, RBC Capital Markets

Our take on the Phase II data: We view the modest percentage weight decrease in these PWS patients as more reflective of the specific patient cohort than the efficacy of beloranib. PWS subjects in institutional group homes are strictly monitored in addition to being on very restrictive diets to control their weight and obesity. These interventions may have already provided benefit to these patients as the average BMI (31.4 ± 5.3 kg/m^2) is already very close to the borderline for definition of obesity, and the range of excess weight was from 1.8 kg to 43.3 kg. Beloranib may be more likely to elicit significant weight reductions in a PWS population that is more obese.

However, in regards to hyperphagia, PWS patients responded quite well to beloranib with negligible side effects. Regarding the one episode of psychotic disorder, we were told by both management and by physicians who participated in the trial that the patient had a prior history of psychosis, with recent life changes and infection resulting from a surgery prior to enrolling in the trial perhaps also playing a role. However, this does bring up a potential safety signal to monitor in beloranib-treated patients. PWS individuals who have uniparental disomy of chromosome 15 (approximately 25% of the PWS population), such as the patient in the Phase II study, have approximately an 85% lifetime risk of psychosis. Thus, this will remain a safety issue to consider, but the subsequent Phase III trial will stratify patients based on genetic mutation in order to follow whether beloranib increases any risk for psychotic episodes.

Patients reported significant decreases in hunger-related behaviors. If approved, this mitigation of hunger would significantly improve patients' quality of life and complement beloranib's other benefits in combating weight gain.

2) Phase III bestPWS trial in obese subjects with PWS

- *Started in September 2014*
- *Expected six-month primary data in YE15*
- *Estimated completion in November 2015*

Study design: The Phase III bestPWS (beloranib efficacy safety and tolerability in PWS, formerly ZAF-311) trial is a randomized, double-blind, placebo-controlled study to investigate beloranib further for the treatment of hyperphagia and reduction of weight in PWS individuals. From 14 sites in the US, 102 patients will be randomized 1:1:1 to receive six months of treatment of placebo, 1.8 or 2.4 mg beloranib subcutaneous injection twice weekly. The protocol will call for beloranib to be administered by trial nurses sent to patients' homes in order to ensure 100% treatment compliance within the trial period. Weight loss and other markers will be assessed for clinical benefit at six months. Patients who complete the randomized treatment will have the option to enroll in an open-label treatment extension for another six months (with a separate trial protocol ZAF-311E). There has been no mention of lifestyle interventions in support of the beloranib treatment protocol.

Patient population: Zafgen will enroll approximately 102 patients with PWS for this trial. In contrast with the Phase II ZAF-211 trial, the Phase III trial seeks to treat PWS patients as young as age 12, who live mostly in a home setting. PWS patients will not be recruited extensively from group homes (as in the Phase II) and will be limited to living <50% of their time in a group home. For adult subjects between the ages of 18 to 65, the inclusion criteria for BMI will be from 30-60 kg/m^2. Adolescent patients must have BMI in ≥95th percentile, based on age and gender. Patients with type 2 diabetes will be allowed as well.

The trial will include only patients with a baseline score of at least 13 on the Dykens questionnaire. Management indicated that the Dykens test is constructed such that

individual PWS patients will need to be similar in severity (though not necessarily in the same metrics or sub-score) in order to reach a score of 13. They do not expect a high screening failure due to this exclusion criterion.

Endpoints: The co-primary endpoints for the study include change in total body fat mass (as measured by DEXA) and change in hyperphagia-related behavior (as measured by the Dykens questionnaire) at the end of beloranib treatment. These two endpoints previously demonstrated statistically significant changes, as compared to placebo, in the Phase II trial. The Dykens test for bestPWS will be following only nine questions versus 10 in Phase II ZAF-211. The one question that was removed was determined by the FDA to have less relevance, as it focused more on effect on the caregivers' quality of lives, versus effects on the patients themselves.

Each of the endpoints is powered at greater than 90% to show efficacy on either one with an alpha of 0.025 for each. To qualify a successful trial, at least one of the two endpoints must be met.

The list of secondary endpoints include change LDL cholesterol, change in HDL cholesterol, total body mass change (by DEXA), change in body weight, change in triglycerides, and quality of life assessment for patients and caregivers.

Comments: Zafgen will request for priority review for beloranib, given the unmet medical need in PWS patients. Talks with the FDA indicate that approval may be subject to positive data with either co-primary endpoint. However, management indicates that it is putting more weight on the Dykens test for hyperphagia. In its interactions with patients and caregivers, Zafgen indicates hyperphagia as the underlying issue that must be addressed in order to gain maximal traction within the patient community.

The bestPWS trial represents one of an anticipated two clinical trials for the beloranib Phase III program. The other trial is to be conducted in Europe, with final details subject to ongoing discussion with the European Medicines Agency (EMA). Zafgen indicates data from both the US and European trials will be included in the FDA submission. Overall, the Phase III program is expected to enroll a combined 250 patients of at least 12 years of age with BMI >30 kg/m^2. The European trial, ZAF-312, is expected to start in mid 2015 and will study the 1.8 mg and 2.4 mg beloranib doses versus placebo for over twelve months of treatment in about 150 PWS patients. The trial will be followed by an open label extension for an additional 6 months of treatment. Zafgen suggests its dialogue with the EMA indicates the EMA's differing views with the FDA regarding the utility of the change in body fat endpoint. Therefore, we believe the European trial may only include the Dykens test as the primary endpoint.

Will the Phase III bestPWS trial succeed?

The success of the Phase III bestPWS trial will hinge on its trial design. Close inspection of the Phase II ZAF-211 and Phase III bestPWS trials in PWS subjects reveal many differences in trial setup and design. Although that potentially raises many red flags, we believe the changes actually maximize the trial's chances to succeed. In the following table, we outline the differences between trial designs for the Phase II and III beloranib PWS trials. Chief among the differences are the following: 1) patient population, 2) beloranib doses and length of treatment, and 3) primary endpoints.

Exhibit 18: Differences between Ph II ZAF-211 and Ph III bestPWS trials in obese PWS subjects

Trial Name	ZAF-211	bestPWS (ZAF-311)
Stage	Phase II	Phase III
Indication	obese PWS	obese PWS
Design	randomized, double-blind, placebo controlled	randomized, double-blind, placebo controlled
Clinicaltrials.gov identifier	NCT01818921	NCT02179151
# of patients	17	102
Starting Date	June 2013	September 2014
Completed	November 2013	6 month data by YE15
Length of treatment	**4 weeks**	**6 months**
Administration	twice weekly subcutaneous injections	twice weekly subcutaneous injections
Treatment arms	placebo, **1.2, 1.8 mg;** open label treatment for 4 weeks at 1.8 mg	placebo, **1.8, 2.4 mg**
Primary endpoints	percent change in body weight	**change in total body fat mass (DEXA), change in hyperphagia (Dykens)**
Secondary endpoints	change in body weight (kg), **change in hyperphagia behavior (Dykens), change in body fat mass**	change in LDL, HDL, total body mass by DEXA, change in body weight, change in triglyceride, quality of life
Inclusion criteria	PWS, **BMI 26-44**, T2DM, **residents of group home, Ages 16-65**	PWS, **baseline Dykens >13**, **Ages 12-17**: BMI ≥95th percentile, Ages 18-65: **BMI 30-60,**
Exclusion criteria	T1DM	**living in group home ≥50% of the time**

Source: Company reports, clinicaltrials.gov

Although these differences will introduce new variables into the PWS trial design, we believe these changes should add to the overall confidence for trial success. **There are four reasons why we believe alterations to the trial design should remove some of the concerns stemming from the Phase II results**.

Reason #1: **We believe Zafgen's PWS strategy is clear with the design of the Phase III bestPWS trial—focus on what worked and stray away from what did not**. Clearly, the modest 1% weight loss (primary endpoint in ZAF-211) seen in group-home PWS individuals living on a restrictive diet and environment did not elicit the most glamorous reduction in weight loss for beloranib-treated patients. That is in contrast with better indicators of beloranib benefit such as the 56% reduction from baseline in hyperphagia-related behavior and a 4% reduction in total body fat mass, which were both statistically significant and are now incidentally the co-primary endpoints. Change in body weight will still be followed as a secondary endpoint.

Reason #2: Although the patient population is different, we believe the focus is being shifted to a higher BMI population where the effects on weight loss of beloranib may be better observed. Moreover, these PWS individuals are not as exposed to the extremely rigid lifestyle restrictions of a group home while living at home, where they are able to access more food and it is harder to maintain a healthy weight. This is more likely to result in a better separation between placebo and treatment arms. Zafgen is citing the PWS patient population who is not institutionalized as a bigger unmet medical need, as group homes provide some health benefits with their rigid lifestyle regimen. However, we believe this choice of patient population is a bigger indictment on management's concern of a predominant group-home patient population. These patients may draw health benefits from such a rigid environment, as seen by lower average BMI (31 kg/m^2) in Phase II ZAF-211 versus a general PWS individual (average BMI >35 kg/m^2) or other obese individuals from Zafgen's other trials (average BMI >36 kg/m^2). The revised inclusion criteria for the Phase III trial also raise the lower BMI limit to 30 kg/m^2 from 25 kg/m^2 in Phase II ZAF-211.

Reason #3: Additionally, a home environment may decrease the volatility seen within the Dykens hyperphagia questionnaire. The nature of the Dykens questionnaire calls for caretakers to comment on the recent two-week food-seeking behavior of the PWS individual. Although those individuals are closely monitored in a group-home setting, the frequent turnover of caretakers may affect consistency of Dykens scores. In a home setting, the caregivers (e.g., parents) responsible for reporting on the PWS individual are more likely to remain constant and, thus, yield more consistency in the subjective questioning format of the Dykens test. Despite this factor, it is important to note that statistical significance was still seen in the improvement of Dykens total score in the 1.8 mg beloranib cohort in the previous Phase II trial.

Reason #4: Zafgen is bringing out the big guns with the incorporation of the 2.4 mg dosage. In prior studies of beloranib on general obese individuals, the 2.4 mg dosage elicited the best weight-loss efficacy seen with beloranib, but came with added side effects, such as sleep disturbances and gastrointestinal events (e.g., nausea and vomiting) that led to study discontinuation in 21 out of 36 general obese individuals. Zafgen cites the inherent hypersomnolent nature of PWS individuals, who tend to fall asleep very quickly with low latency, in addition to their very insensitive GI system as reasons to lessen safety concerns of the 2.4 mg dosage in this patient population. Management presumes that these characteristics of PWS individuals should shield them from the same adverse effects in sleep disturbances and GI issues seen at >2 mg doses in other general obese individuals. Moreover, these side effects tend to dissipate over time with continuous treatment, and the protocol plans to titrate the drug for the first few weeks of treatment to allow the patient to acclimate to the beloranib treatment.

What is next for beloranib in PWS?

Zafgen guided that it expects the first six-month data from the bestPWS trial to be released by 4Q15. This would suggest full results in 2016, followed by a New Drug Application (NDA) submission. The company would also include data from its planned Phase IIb trial in general obese individuals to supplement the safety database surrounding beloranib treatment.

The current intended PWS population for beloranib would be limited to those over the age 12, as outlined in the Phase III bestPWS trial. However, the company suggests its ultimate goal is to expand treatment into patients as young as five to seven, who may be just approaching the hyperphagic stage. It cites the medical need in these patients and parents' desires to prevent the consequences, both physically and behaviorally, of the hyperphagic stage.

The company suggests that once preliminary safety data are available in adolescent PWS patients (from the bestPWS trial), it can start plans for dosing younger patients. Safety studies will need to be performed in juvenile studies, and formal Pharmacokinetic and Pharmacodynamic (PK/PD) studies will be needed to confirm the proper dosage of beloranib in younger patients. Also, label expansion into the pediatric population may not need complete efficacy data.

Competitors' trials in PWS patients

As bariatric surgery is contraindicated in PWS patients, the need is greater for pharmacological agents to modulate hunger and hyperphagia-related behaviors in patients with PWS. Besides Zafgen, a few other companies and groups are pursuing therapies for use in PWS.

Essentialis is conducting a single-center, open-label, single-arm, Phase I study of a diazoxide choline controlled-release tablet (DCCR) for treating PWS individuals from age 10 to 20 years. Again, the primary endpoint in the proposed 12 patients will be hyperphagia using a questionnaire. Essentialis announced in May 2014 that it received an orphan drug designation for diazoxide choline for the treatment of PWS. Treatment with diazoxide choline is thought to target the KATP channel within neurons to impact on hypothalamic control of food intake and energy expenditure. It is also suggested that DCCR can affect de-novo lipogenesis and β-oxidation of fat.

In addition, Rhythm Pharmaceuticals announced a plan to start a Phase IIa trial of RM-493, a first-in-class melanocortin-4 (MC4) receptor agonist, in PWS patients. The MC4 pathway is believed to play an important role in energy metabolism, homeostasis, and food intake in humans. Unlike first-generation, small-molecule, MC4 receptor agonists, RM-493, a peptide targeting MC4 receptor, does not affect blood pressure. Besides the trial in PWS patients, RM-493 will be tested for treating obesity in people with a mutation in their MC4 receptor as well.

As GH has yielded benefits to children with PWS who experience growth failure, studies are launched to develop either better GH or extend the use of GH. In a Phase III study in South Korea, LG Life Science is evaluating the efficacy and safety of Eutropin compared to Genotropin in infants and toddlers with PWS. Eutropin is a recombinant HG hormone for the treatment of short stature with various indications. In a Phase I/II trial sponsored by independent investigators, Oxytocin, a human GH is being tested in infants with PWS from one- to five-months old.

PWS patients have been found to have oxytocin-producing neuron deficiency and reduced oxytocin receptor gene activities. To address the benefits of oxytocin in PWS patients, an ongoing Phase I trial is led by a research team at the University of Florida and the US National Institute of Health (NIH) to investigate the safety of oxytocin administration in PWS patients between 5- and 11-years old. Additional outcomes will measure whether oxytocin can improve patients' food-seeking behaviors. A previous placebo-controlled study in 24 adult PWS patients showed that, after a single intranasal oxytocin admistration, patients significantly increased trust in others with less disruptive behaviors. In addition, Ferring Pharmaceuticals is assessing hyperphagia behavioral symptoms with its FE992097 treatment (an intranasal oxytocin analogue) versus placebo in 38 patients with PWS. That Phase II study is exploring as a primary endpoint of change in total hyperphagia score over the course of 15 days in patients 10- to 18-years old.

Hypothalamic injury-associated obesity (HIAO)

Whereas PWS is a genetic disorder that has implications on hypothalamic control of hunger, direct, physical alterations, or injuries to the hypothalamus can also result in obesity. Zafgen refers to these unique patients as those who suffer from hypothalamic injury-associated obesity, or HIAO. Chief among medical situations that result in hypothalamic injury is the case of craniopharyngiomas and, specifically, the surgical treatment of it, which account for 80-90% of HIAO cases. Other less common causes may include strokes, brain trauma, and radiation therapy to the brain.

Craniopharyngiomas (CPs) are rare benign tumors with an incidence of 0.5 to 2.0 cases per million per year and a prevalence of about 1 in 50,000. This correlates to about 6,000 and 10,000 individuals with craniopharyngiomas in the US and EU, respectively. Of these patients, an estimated 50% will develop morbid obesity following treatment. Tumors typically arise in the parasellar and suprasellar regions near the vicinity of the hypothalamus and exhibit a bimodal age distribution in patients. Approximately half of cases arise in children and the other half in adults from 50 to 74 years. Long-term survival rates can be high with an 87-95% 20-year survival in childhood-onset patients, although adult-onset patients have much higher mortality rates as compared to the general population.

While the CPs themselves are benign, they inhabit a critical region and are usually life threatening if left untreated. Treatments for the disease primarily include surgery and/or radiation therapy. However, the process of treating these tumors, which are surrounded by very delicate neural tissues, often leads to long-term serious consequences and impaired quality of life. These morbidities include pituitary dysfunction, visual deterioration, and seizures due to the tumor's proximity to the optic nerve and/or chiasma and hypothalamic-pituitary axes. Moreover, patients frequently suffer from obesity and show other signs of metabolic syndrome, contributing in part to the increased morbidity and mortality of patients post-treatment.

Increased daytime sleepiness and reduced melatonin secretion at night are also common, perhaps due to hypothalamic dysfunction and interference with the suprachiasmatic nucleus of the hypothalamus that regulates sleep and circadian rhythms. Many CP patients rely on others for daily activities due to limited physical function and mobility issues.

Obesity in patients with hypothalamic injury

Initial evidence for damage to the hypothalamus leading to obesity comes from a rat model that has been used experimentally for approximately 50 years. Damaging the area of the brain known as the ventromedial hypothalamus (VMH) induces non-stop eating and weight gain in these rats. Enforcing severe caloric restriction in these rats with VMH damage does not diminish the weight gain, because their metabolism is thought to favor energy storage instead of energy burning.

In human patients, support for a connection between hypothalamic injury and obesity comes from a study of children who developed obesity after surviving brain tumors. The study identified factors that affected the onset of obesity to include the following: 1) tumor location (i.e., hypothalamus), 2) tumor histology (craniopharyngioma and hypothalamic astrocytoma), 3) surgery, 4) amount of radiation directed at the hypothalamus (>51 Gy), and the presence of hypothalamic hormone disturbances. These results implicated the damage on the hypothalamus during brain tumor treatment as the source of obesity.

Reports of CP patients also describe a significant reduction in physical activity and basal metabolic rate, pointing to reduced energy expenditure rather than high-energy intake as causes of obesity. For example, the caloric intake of patients with CP is not reportedly higher than that of control individuals with general non-hypothalamic obesity, but physical activity was reduced.

In childhood-onset cases, weight gain frequently occurs before CP diagnosis, with 12 to 19% of patients reporting to be obese at the time of diagnosis. Weight gain cannot be offset through adequate endocrine replacement of pituitary hormone deficiencies in these patients. However, rapid weight gain often transpires during the first six to 12 months after surgery or radiation treatment, and the rates of obesity increase up to 55% post-treatment. Altogether, obesity in CP patients increases the risk of metabolic syndrome and cardiovascular disease, resulting in multisystem morbidities and increased mortality.

Phase IIa ZAF-221 trial in obese subjects due to hypothalamic injury

- *Study started in June 2014*
- *Patient enrollment completed September 2014*
- *Positive top-line data released January 2015*

Study design: The Phase IIa ZAF-221 trial is a randomized, double-blind, placebo-controlled trial to assess the efficacy of beloranib in treating hyperphagia and obesity in patients with hypothalamic injury, mostly due to treatments treating craniopharyngioma (such as trauma from brain surgery or radiation treatment). Patients were randomized to receive placebo or 1.8 mg beloranib twice-weekly subcutaneous injections for four weeks, followed by a four-week, open-label extension.

Patient population: From two US and two Australian centers, 14 obese patients with radiographically confirmed hypothalamic damage were recruited for the study. Patients aged 18 to 65 must be obese due to hypothalamic injury, with a BMI of 30-60 kg/m^2, and must be more than six months removed from tumor treatment. Patients who have undergone bariatric surgery or females who are planning to become pregnant within six months of the trial were excluded from enrollment.

Endpoints: The primary endpoint for the study is the change in body weight at four weeks. Secondary endpoints will include changes in lipid profile, high-sensitivity C-reactive protein (hs-CRP), hunger, and quality of life from baseline to the end of the four-week, randomized dosing period.

Positive results from the Phase II trial in HIAO patients leads to a second rare disease indication for beloranib, with the potential to double its market opportunity.

Results: Despite the small trial, treatment with beloranib resulted in statistically significant weight reductions in HIAO patients. The mean weight loss in beloranib-treated patients were 3.4 kg and 6.2 kg after 4 and 8 weeks, respectively, versus a 0.3 kg mean weight loss at 4 weeks in patients treated with placebo (p=0.01). In addition, improvements in the cardiovascular risk factor of C-reactive protein were exhibited. No new safety signals were seen in the patients in the trial.

Comments: The second rare indication targeted by Zafgen is obesity resulting from hypothalamic injury, which the company labels as HIAO and sometimes as “acquired PWS”. Although small, the Phase II trial provided positive results indicating efficacy of beloranib in this patient population with a definite unmet medical need. Considering there is no other treatment that works in these patients, we believe beloranib can be of significant benefit in this patient population. The trial’s success warrants further study of beloranib in this second rare disease indication, which we believe to have a market opportunity equivalent of the one in PWS.

Beloranib for the treatment of general obese individuals

Thus far, Zafgen have conducted three Phase Ib studies of beloranib in obese women. Additionally, one Phase II trial has expanded the study into both men and women, with an additional Phase II trial initiated in December 2014.

Exhibit 19: Summary of beloranib clinical trials in general obese patients

Trial Name	Phase Ib ZAF-001	Phase Ib ZAF-003	Phase Ib ZAF-101	Phase IIa ZAF-201
Design	randomized, double-blind, placebo-controlled	randomized, double-blind, placebo-controlled	randomized, double-blind, placebo-controlled	randomized, double-blind, placebo controlled
clinicaltrials.gov	NCT01028261	NCT01372761	NCT01507077	NCT01666691
Patient population	obese women	obese women	obese women	obese patients
# of patients	31	16	25	160
Starting Date	Dec 2009	June 2011	Dec 2011	Aug 2012
Completed	Oct 2010	Nov 2011	March 2012	May 2013
Length of treatment	4 weeks	4 weeks	4 weeks	12 weeks
Administration	twice weekly IV	twice weekly IV	twice weekly subcutaneous	twice weekly subcutaneous
Treatment arms	placebo, 0.1, 0.3, 0.9 mg	placebo (n=5), 3.0 (n=6), 6.0 mg (n=5)	placebo (n=6), 1.0 mg (n=6), 2.0 (n=6), 4.0 (n=7)	placebo, 0.6, 1.2, 2.4 mg
Primary endpoints	safety and tolerability	safety and tolerability	safety and tolerability	safety and tolerability, weight loss
Secondary endpoints	weight (2 months)	weight loss		PD, PK, bioavailability
Average weight loss	median weight loss 0.9 mg: -3.8 kg; placebo: -0.6 kg	3.0 mg: -4.7 kg (p=0.0008); 6.0 mg: -6.7 kg (p=0.0013); placebo: +0.2 kg	1.0: -4.3 kg; 2.0: -4.2 kg, 4.0 mg: -6.1 kg, placebo: -1.2 kg (all p<0.001)	0.6 mg: -5.3%; 1.2 mg: -6.7%; 2.4 mg: -10.6%
Biomarkers	decreases in C-reactive protein and metabolic hormones			significant decreases in leptin and C-reactive protein; increase in adiponectin
Safety	137 TEAEs (94% of patients), headache most frequent (more in placebo group)	mild diarrhea, nausea, headache, dizziness, infusion site injury, mild-to-moderate sleep disturbance	mostly GI side effects and sleep disturbances, decreased appetite, vivid dreams, sleep disturbance	**most AEs above 2 mg**; sleep disturbance (increased sleep latency), nausea, vomiting; mild/moderate intensity and short in duration

Source: Company reports, clinicaltrials.gov

1) Phase Ib ZAF-001 in obese women

- *Study started December 2009*
- *Study completed October 2010*
- *Results published in Obesity February 2013*

Study design: The first of three Phase Ib studies, ZAF-001 is a randomized, double-blind, placebo-controlled trial to study beloranib in obese female volunteers. Patients received placebo, 0.1 mg/m^2, 0.3 mg/m^2, or 0.9 mg/m^2 twice-weekly via IV for four weeks.

Patient population: 31 female obese volunteers (mean BMI 38 kg/m^2) were recruited across sites in Australia. Eligible participants were non-diabetic, aged 18-60 years (average age of 52.2 years), at least 50 kg in weight, and had BMI between 32 and 45 kg/m^2.

Endpoints: The primary endpoints were safety and tolerability, and the secondary endpoint followed weight change.

Efficacy: After four weeks of beloranib treatment, the median weight loss observed was -3.8 kg in the 0.9 kg/m^2 dose versus -0.6 kg in placebo. The other two dosages reported similar weight change as seen with placebo. The highest dose of beloranib (0.9 kg/m^2) was also associated with a significant 42% and 18% decrease in triglycerides and LDL 'bad' cholesterol. There was also a dose-dependent benefit in metabolic markers (C-reactive protein and metabolic hormones).

Safety: 29/31 (94%) of volunteers reported a total of 137 adverse events, mostly mild or moderate in severity. The most frequent complaint was headaches, but with greatest incidence occurring in the placebo group. Others included infusion site injury, nausea, and diarrhea. No dose-limiting toxicities or deaths were reported associated with beloranib.

2) Phase Ib ZAF-003 in obese women

- *Study started June 2011*
- *Study completed November 2011*

Study design: The second of beloranib's three Phase Ib trials in obese women increased the dosages of beloranib from the first Phase Ib trial. The randomized, double-blind, placebo-controlled trial tested placebo against 3.0 mg/m^2 or 6.0 mg/m^2 beloranib twice-weekly IV for four weeks.

Patient population: The second trial enrolled 16 obese Australian women and randomized five women to placebo, 6 to 3.0 mg/m^2, and 5 to 6.0 mg/m^2. The inclusion criteria for BMI were 30-50 kg/m^2, and the average BMI of patients in this study was 39.5 kg/m^2.

Endpoints: The primary endpoints were safety and tolerability, and the secondary endpoint followed weight change.

Efficacy: At four weeks, there were significant weight losses of 4.7 kg (at 3.0 mg/m^2, p=0.0008) and 6.7 kg (at 6.0 mg/m^2, p=0.0013) versus a gain of 0.2 kg for the placebo group. Additionally, hunger was reduced by 28% (3.0 mg/m^2) and 52% (6.0 mg/m^2) in the beloranib cohorts, and by 2% in the placebo group.

Safety: At the increased beloranib dosages, the adverse effects consisted of mild diarrhea, nausea, headache, dizziness, infusion site injuries, and mild to moderate sleep disturbances.

Comments: A separate arm to the trial tested 2.5 mg given twice weekly for the first week and once weekly for the subsequent six weeks. The once-weekly regimen was ruled out and determined to be less effective than the twice-weekly administration.

3) Phase Ib ZAF-101 in obese women

- *Study started December 2011*
- *Study completed March 2012*

Study design: The final Phase Ib beloranib trial in obese female volunteers was the first trial to study beloranib as a twice-weekly subcutaneous injection (the current administration method). This randomized, double-blind, placebo-controlled trial assessed efficacy of placebo versus 1.0 mg, 2.0 mg, and 4.0 mg of beloranib for four weeks.

Patient population: The study enrolled 25 non-diabetic patients with non-childbearing potential and an average BMI of 34-36.4 kg/m^2 across the treatment groups.

Endpoints: The primary endpoints were safety and tolerability, and the secondary endpoint followed weight change.

Efficacy: At four weeks, the average weight loss was 4.3 kg (1.0 mg), 4.2 kg (2.0 mg), and 6.1 kg (4.0 mg). These were all statistically significant (all p<0.001) compared to placebo, which had a weight loss of 1.2 kg. The sensation of hunger was reduced by 42% (1.0 mg), 45% (2.0 mg), 46% (4.0 mg), and 22% (placebo).

Exhibit 20: Weight loss in ZAF-101 trial (four weeks of treatment)

Trial Arm	# of Patients	Baseline Body Weight (kg)	Average Weight Change (kg)	% Placebo-Adjusted Weight Change	p-value
Placebo	6	97.3	-1.2	----	----
Beloranib 1.0 mg	6	99.1	-4.3	-3.1%	p<0.001
Beloranib 2.0 mg	5	92.7	-4.2	-3.3%	p<0.001
Beloranib 4.0 mg	4	93.9	-6.1	-5.3%	p<0.001

Source: Company reports, RBC Capital Markets

Safety: Common adverse effects reported were decreased appetite, vivid dreams, and other sleep disturbances. Sleep disturbances caused four participants to withdraw from the trial: three from the 4.0 mg treatment group and one from the 2.0 mg treatment group.

Comments: The results of the ZAF-101 trial confirmed twice-weekly subcutaneous administration as the clinical administration for beloranib going forward. Despite strong efficacy of the 4.0 mg dose, this dose was not as well tolerated with side effects mainly observed relating to gastrointestinal effects and sleep disturbances.

4) Phase IIa ZAF-201 in obese individuals

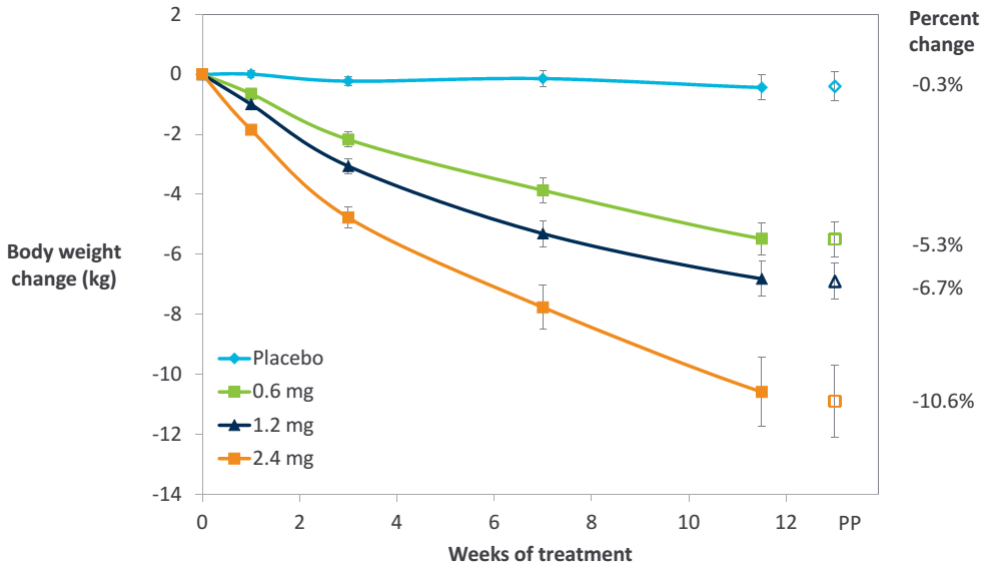
- *Study started August 2012*
- *Study completed May 2013*

Study design: The randomized, double-blind, placebo-controlled Phase IIa ZAF-201 trial in general obese subjects tested twice-weekly subcutaneous beloranib injections versus placebo for 12 weeks. The trial enrolled 160 subjects across eight sites in Australia. No lifestyle interventions were included in the weight-loss protocols for both groups. Beloranib was tested in dosages of 0.6 mg, 1.2 mg, and 2.4 mg. Two additional treatment doses, 0.3 mg and 3.2 mg, were ruled out and eliminated after the first two four-week dosing (pre-defined decision) due to being not effective and not well tolerated, respectively.

Patient population: The subjects had an average BMI of 38 kg/m^2 (range 30-54 kg/m^2). Patients with type 2 diabetes mellitus were also allowed for the first time in a beloranib study. The majority of enrolled subjects (93.8%) were women, and 122 were dosed with beloranib.

Endpoints: The primary endpoints were safety, tolerability, and weight loss. Secondary endpoints included PD, PK, bioavailability, and other biomarkers.

Exhibit 21: Body weight change for Ph IIa ZAF-201 trial



Source: Company reports

Weight loss efficacy: The placebo-adjusted percentage change in weight loss was 5.0% (0.6 mg), 6.4% (1.2 mg), and 10.3% (2.4 mg) at 12 weeks. Weight loss at each dose was statistically significant.

Exhibit 22: Weight loss in ZAF-201 trial (12 weeks)

Trial Arm	# of Patients	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%	p<0.0001
Beloranib 1.2 mg	31	102.6	-6.9	-6.3%	p<0.0001
Beloranib 2.4 mg	15	102.2	-10.9	-10.3%	p<0.0001

Source: Company reports

Decreases in biomarkers were also exhibited, especially at higher doses of 1.2 mg and 2.4 mg. Levels of the cardiovascular disease risk marker C-reactive protein (also used as a marker of inflammation) were lower in patients treated with beloranib. Patients demonstrated a reduction in systolic blood pressure of 6.3 mmHg, 6.3 mmHg, and 13.6 mmHg with beloranib treatment at 0.6 mg, 1.2 mg, and 2.4 mg, respectively, as compared to an average reduction of 1.4 mmHg in patients treated with placebo. However, diastolic blood pressure only demonstrated trends toward reduction, with no statistical significance achieved.

Exhibit 23: Secondary markers following beloranib treatment in ZAF-201

Change in Marker	Placebo (n=36)	0.6 mg Beloranib (n=34)	1.2 mg Beloranib (n=31)	2.4 mg Beloranib (n=15)	p-value
% change leptin (Completers)	+12.0%	-37.0%	-45.0%	-57.0%	all p<0.001
% change adiponectin (Completers)	-3.0%	+48.0%	+68.0%	+81.0%	all p<0.001
% change in hunger (Completers)	+10.5%	+7.1%	-32.8%	-52.2%	all p<0.05
C-reactive protein (µg/ml)	+1.0	-2.5	-2.3	-1.9	all p<0.0001
% change C-reactive protein	----	-23.0%	-22.0%	-37.0%	
LDL cholesterol (mmol/L)	-0.3	-0.3	-0.5	-1.0	2.4 mg: p<0.001
% change LDL-c	----	-9.4%	-14.5%	-29.7%	
HDL cholesterol (mmol/L)	0	+0.1	+0.1	+0.2	1.2 and 2.4 mg: p<0.05
% change HDL-c	----	+7.6%	+11.6%	+14.6%	
Triglycerides (mmol/L)	-0.3	-0.2	-0.3	-0.4	1.2 and 2.4 mg: p<0.05
% change triglycerides	----	-8.8%	-9.0%	-20.3%	
Systolic blood pressure (mmHg)	-1.4	-6.3	-6.3	-13.6	1.2 mg and 2.4 mg: p<0.05

Source: Company reports, RBC Capital Markets

Safety: The trial noted that most adverse events occurred at doses above 2 mg. The most common adverse event (AE) leading to trial withdrawal was sleep disturbance, with 21 patients in the 2.4 mg cohort withdrawing, mostly due to reported sleep disturbances stemming from increased sleep latency. Other classes of side effects included gastrointestinal symptoms (i.e., nausea, diarrhea, and vomiting), nervous system (i.e., dizziness), and psychiatric disorders (i.e., insomnia, sleep disorder, and abnormal dreams). The side effects were generally mild to moderate in intensity, short in duration, benign, and fairly manageable. Although there were no deaths or serious adverse event, there were two serious thrombotic adverse events, not attributed to beloranib, but it still points to caution in future beloranib trials when enrolling individuals with a prior history of thrombotic events.

Comments: The ZAF-201 met its primary endpoints and suggested efficacy of beloranib in treating general obese individuals. Moreover, the study suggested that beloranib treatment not only does not increase the risk of cardiovascular disease, which obese patients are at increased risk for, but also it may be associated with reduced cardiovascular disease risk. Many obesity drugs have been mandated to perform extra safety trials, especially for cardiovascular outcomes. Beloranib's reduced cardiovascular risk (if held up over long-term use) may lessen one of the safety concerns commonly associated with obesity drugs and remove an additional hurdle to regulatory approval.

5) Phase IIb ZAF-203 in severe obese individuals

- *Study started 4Q14*
- *Six-month interim data expected in 4Q15*

Study design: This study will enroll approximately 160 patients across 15 sites and randomized them 1:1:1 to receive placebo, 1.2 mg, or 1.8 mg beloranib, as twice-weekly subcutaneous injections.

Patient population: The patient population will be exclusively obese adults with a co-morbidity of type 2 diabetes. Patients will have BMI from 30-50 kg/m^2.

Endpoints: The primary endpoint in the study is weight loss at 6 and 12 months.

Comments: Zafgen is continuing the beloranib program in general obese individuals in this Phase IIb trial. Moreover, safety data from this trial will supplement the overall beloranib safety database, to be used potentially for beloranib in PWS registration. Trial details are still being updated, only focusing on diabetic patients who may be most interested in beloranib (according to Zafgen KOL discussions) and are familiar with injectable drugs.

Management indicates that the trial may potentially focus on severe or super-severe obese patients, as defined by a BMI >40 and >50, respectively. However, strategies are still under discussion as to how to carry beloranib forward in general obese individuals or those with specific BMIs. The scenarios mentioned are the following: 1) if beloranib demonstrates positive data in PWS, then beloranib may be reserved only for orphan diseases with a follow-on molecule to target general obese individuals, and 2) if beloranib demonstrates negative data in PWS, then the program would shift its focus to either general obese or perhaps a subset of severe and/or super-severe obese individuals.

We view this as a binary decision, and as of now, we believe beloranib will follow scenario #1 and be indicated only for patients with orphan diseases. In such a case, we anticipate Zafgen to accelerate its early stage program to identify a follow-on MetAP2 inhibitor that it would fully own to target obesity in the general population. This program would be a few years behind, but it anticipates to offset that time lag with the following advantages: 1) full economic rights to the program and 2) parsing out some chemical properties of beloranib, in order to reduce adverse events seen with beloranib. However, as of now, Zafgen indicates the follow-on molecule to be also an injectable, with most likely a twice per week dosing regimen.

Summary of Beloranib safety issues

Given the difficulty history of anti-obesity pharmacotherapies, safety remains a very sensitive issue as the FDA continues to monitor any safety risk associated with weight loss drugs in clinical development. Scrutiny of every candidate drug is expected, and any reported safety issue with beloranib will be closely reviewed.

Preclinical toxicology studies of beloranib have been conducted in beagle dogs, rats, and rabbits. Data from Zafgen's dog studies have indicated hypospermatogenesis (low sperm counts), lowering of platelets, decreased white blood cell counts, gastrointestinal bleeding, and seizures, but all of these occurred at doses above the indicated human doses. Further studies in rats have also observed sporadic and reversible reduction in sperm counts and cellular changes in the testes at beloranib levels 10- to 15-fold above the male human exposure levels seen in the ZAF-201 trial. Although no parallel spermatogenesis issues have been reported in male subjects thus far, this issue will continue to be closely followed. This

signal should not be an issue in male PWS patients, as these individuals are infertile and suffer from hypogonadism.

In the Phase 2a clinical trial (ZAF-201) of beloranib in general obese patients, the major adverse event that has led to treatment discontinuation was sleep disturbances, mainly presented as delayed onset of sleep. Other main adverse events included nausea and vomiting. According to the company, there have been no serious adverse events attributed to beloranib in the clinical trials.

As with other anti-obesity drugs, we expect beloranib, if approved, to carry a Pregnancy Category X label and to be contraindicated in pregnant women or women looking to become pregnant.

Competing drugs for weight loss/obesity

Since the 2007 release of the FDA's new draft guidance on obesity drugs, four new weight loss drugs have completed clinical development. Based on meeting either or both the mean and categorical efficacy as dictated by the FDA guidance, these four drugs (Qsymia, BELVIQ, Contrave, and Saxenda) are now approved in the US and have increased the options available to physicians and patients for the treatment of obesity.

Exhibit 24: A snapshot of the four recently approved obesity drugs

	Qsymia	BELVIQ	Contrave	Saxenda
Company	Vivus	Arena	Orexigen	Novo Nordisk
FDA approval	July 2012	June 2012	September 2014	December 2014
US launch	September 2012	June 2013	October 2014	1H 2015
US commercial partner	N/A	Eisai	Takeda	N/A
Sales force (reps)	150	600	900	500
EU approval	pre-approval CVOT required	MAA withdrawn	pending	N/A
Dose	oral phen/topi recommended: 7.5/46 mg high dose: 15/92 mg	oral 10 mg BID	oral 32 mg nal + 360 mg bupropion	3.0 mg subcutaneous injection
MOA	phentermine + topiramate extended-release	lorcaserin (serotonin 2C receptor agonist)	sustained-release bupropion + naltrexone	GLP-1 agonist
Treatment efficacy evaluation	≥3% weight loss after 12 weeks (rec dose)*	≥5% weight loss by week 12	≥5% weight loss by week 12	≥4% weight loss by week 16
Placebo-adjusted weight loss	8.6-9.3%	~3.6%	~4.6%	5.4%
% patients achieving >5% weight loss, vs. placebo	66.7% vs. 17.3%; 70% vs. 21%	47.5% vs. 20.3%	48% vs. 16.4%; 55.6% vs. 17.5%	64% vs. 27%
Post-marketing requirements	CVOT, REMS	CVOT by YE2017	new CVOT	MTC case registry, REMS

*Discontinue or escalate to high dose (15/92 mg)

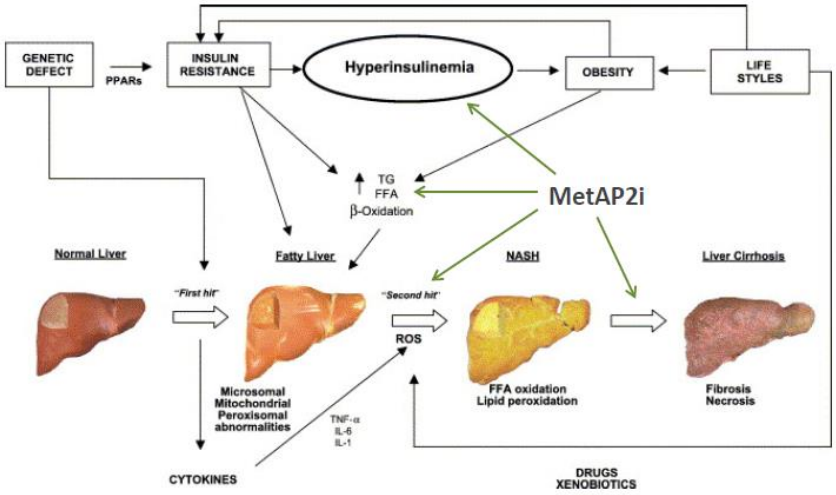
Source: Company reports, RBC Capital Markets

Early stage compound ZGN-839 for NASH and type 2 diabetes

NASH overview

In addition to weight management, MetAP2 inhibitors may have application in the treatment of other metabolic diseases as well, such as nonalcoholic steatohepatitis (NASH), and type 2 diabetes. As shown in the following exhibit, MetAP2 inhibition could rebalance fat metabolism, improve fat oxidation, and increase insulin sensitivity. As fat deposit and free fatty acid oxidation are important factors contributing to NASH, MetAP2 inhibitors could potentially delay the progression of NASH, thereby reducing the risk of liver failure and liver cancer.

Exhibit 25: MetAP2 inhibitors could potentially delay the progression of NASH.



Source: Company reports

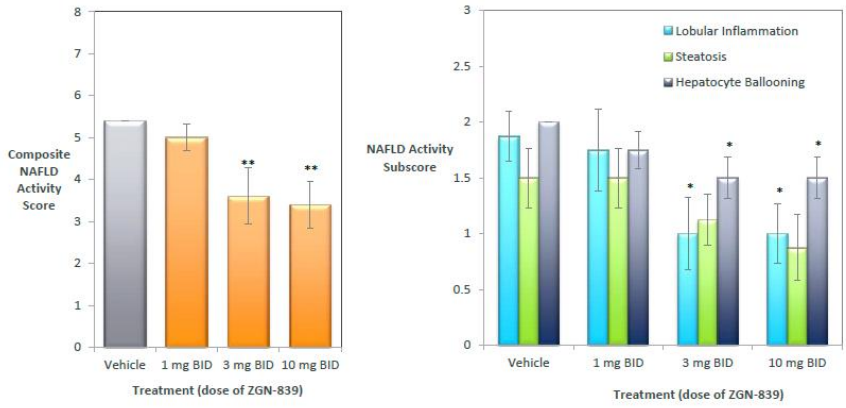
NASH is the extreme form of nonalcoholic fatty liver disease (NAFLD), a spectrum of liver diseases that occur when fat is accumulated in the liver not due to alcohol use. Liver function may be preserved in asymptomatic NAFLD patients, but if NAFLD progresses to NASH, where fat deposition is combined with inflammation in the liver, then liver function becomes disturbed and ultimately leads to liver cirrhosis. Liver cirrhosis is an irreversible process during which liver tissue is replaced by fibrosis. Such continued liver damage in people with NASH may eventually result in liver failure.

In the US, the prevalence of NASH is estimated to be as high as 2-3% of the total population. Studies suggest that between 16-30% of individuals affected by NASH will have a progressive course. These patients would experience liver fibrosis and cirrhosis, and have an increased risk of liver cancer.

Preclinical results of ZGN-839: Potential for the treatment of NASH and diabetes

ZGN-839, an oral MetAP2 inhibitor, was able to reduce the NAFLD score and individual components of the score in a mouse model of NAFLD and liver fibrosis. The NAFLD score, calculated using clinical information and lab data, is used to identify patients whose NAFLD has advanced to liver fibrosis. Low NAFLD scores indicate a low chance for NAFLD progression. In the following exhibit, preclinical data are shown with the Stelic neonatal streptozotocin/high-fat, diet-treated mouse model. Four weeks of daily ZGN-839 treatment (3 mg and 10 mg BID) demonstrated statistically significant reductions in the NAFLD score, as compared to mice receiving only vehicle.

Exhibit 26: ZGN-839 reduced NAFLD score in an NAFLD and liver fibrosis mouse model.



Source: Company reports

In addition to NASH, ZGN-839 is also in preclinical studies for the treatment of type 2 diabetes. In another mouse model of diabetes, ZGN-839 was found to reduce plasma glucose levels. The programs of ZGN-839 in NASH and diabetes are still early, with the potential of an IND submission in the 1H15.

Intellectual property

The US and European composition of matter patents for beloranib are exclusively licensed to Zafgen and will expire in the 2019. Additionally, Zafgen holds two US patents for beloranib polymorph compositions of matter and two US patents related to the treatment of obesity that will expire in 2031 and 2029, respectively. Pending approval, the polymorph composition of matter in Europe will also expire in 2031.

Partnerships

Chong Kun Dan Pharmaceutical

The worldwide exclusive license to beloranib (ex-South Korea) was licensed in July 2009 from Chong Kun Dan Pharmaceutical Corp (CKD) of South Korea. The license grants intellectual property rights of beloranib to Zafgen in return for the following: 1) an initial license fee, 2) a one-time fee following initiation of beloranib proof of concept trial, 3) milestone payments of up to $30MM (of which $7.5MM has been paid), 4) a portion of any sublicensing income, and 5) single-digit royalties based on annual net sales of beloranib on successful marketing approval. The royalties shall expire in each country depending on the later to occur event of either 1) expiration of last to expire patent within that country or 2) 10 years from the first commercial sale of beloranib in that country.

Children's Medical Corporation

Zafgen also possesses an exclusive worldwide license with Children's Medical Center Corporation since January 2007 to pursue undisclosed patent rights relating to decreasing the growth of fat tissue. This licensed patent right covers the use of beloranib and other related compounds as anti-obesity agents. For this license, Zafgen paid an initial license fee and annual maintenance fees for five years succeeding the license agreement. Zafgen is to pay milestone payments to Children's up to $2.7MM (of which $0.4MM has been paid), and up to $1.3MM for each subsequently licensed product and a portion of any sublicensing income. Additionally, on beloranib marketing approval, single-digit royalties based on net sales of beloranib is also due to Children and will last until the later to occur of 1) expiration of last to expire patent in the country or 2) 15 years from the date of the agreement, or January 2022.

Financials

Income statement

For the most recent quarter, 3Q14, the company reported a net loss of $14.7MM, or ($0.65) per share, compared to a net loss of $3.5MM, or ($4.88) per share, in 3Q13.

Total operating expenses equaled $14.4MM in 3Q14 while it equaled $3.5MM in 3Q13. R&D expenses accounted for $12.1MM in 3Q14 and $2.4MM in 3Q13. Zafgen reported 3Q14 G&A expenses of $2.3MM, as compared to $1.1MM in 3Q13.

Balance sheet

Zafgen recorded $127.0MM in cash at the end of 3Q14. A total of 22.7MM common shares are outstanding, with 1.8MM in outstanding options and warrants.

Exhibit 27: ZFGN quarterly P&L ($MM)

($MM)	FY 2013A	Q1: 14A	Q2: 14A	Q3: 14A	Q4: 14E	FY 2014E	Q1: 15E	Q2: 15E	Q3: 15E	Q4: 15E	FY 2015E	FY 2016E
US beloranib PWS 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
US beloranib HIAO 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
Total US beloranib 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**
EU beloranib PWS 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
EU beloranib HIAO 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
Total EU beloranib 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**
Total US/EU beloranib 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**
Royalties paid to CKD Pharma	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Royalties paid to Children's	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 royalties paid	**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 revenue	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**
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**
R&D	**9.6**	**3.3**	**4.7**	**12.1**	**6.7**	**26.7**	**7.2**	**7.1**	**7.7**	**8.1**	**30.1**	**31.9**
SG&A	**4.2**	**1.2**	**1.3**	**2.3**	**2.4**	**7.2**	**2.4**	**2.5**	**2.4**	**2.5**	**9.8**	**10.1**
Total Operating Expenses	**13.8**	**4.5**	**6.0**	**14.4**	**9.1**	**33.9**	**9.6**	**9.6**	**10.1**	**10.6**	**39.9**	**42.0**
Operating Income (loss)	**(13.8)**	**(4.5)**	**(6.0)**	**(14.4)**	**(9.1)**	**(33.9)**	**(9.6)**	**(9.6)**	**(10.1)**	**(10.6)**	**(39.9)**	**(42.0)**
Total other expenses, net	(0.2)	0.1	(0.4)	(0.3)	(0.3)	(1.0)	(0.1)	(0.2)	(0.1)	(0.1)	(1.9)	(3.3)
Net loss and comprehensive loss	(14.0)	(4.5)	(6.4)	(14.7)	(9.4)	(34.9)	(9.7)	(9.8)	(10.2)	(10.7)	(40.4)	(45.3)
Accretion of redeemable convertible stock	(0.2)	(0.0)	(0.0)	0.0	(0.0)	(0.1)	(0.0)	(0.0)	(0.0)	(0.0)	(0.1)	(0.1)
Pretax income	(14.2)	(4.5)	(6.4)	(14.7)	(9.4)	(35.1)	(9.8)	(9.8)	(10.2)	(10.7)	(40.5)	(45.4)
Income tax expense	0.0	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%*	*0%*	*0%*	*0%*	*0%*
Net income (loss)	**(14.2)**	**(4.5)**	**(6.4)**	**(14.7)**	**(9.4)**	**(35.1)**	**(9.8)**	**(9.8)**	**(10.2)**	**(10.7)**	**(40.5)**	**(45.4)**
GAAP EPS												
Basic	($19.53)	($6.18)	($2.96)	($0.65)	($0.41)	($2.90)	($0.37)	($0.38)	($0.39)	($0.41)	($1.55)	($1.45)
Diluted	($19.53)	($6.18)	($2.96)	($0.65)	($0.41)	($2.90)	($0.37)	($0.38)	($0.39)	($0.41)	($1.55)	($1.45)
Basic shares	0.7	0.7	2.2	22.7	22.8	12.1	26.1	26.1	26.2	26.2	26.2	31.3
Diluted shares	0.7	0.7	24.5	24.5	24.5	18.6	27.8	27.9	27.9	28.0	27.9	33.1

Source: SEC Filings, RBC Capital Markets estimates

Exhibit 28: Zafgen annual P&L ($MM)

($MM)	FY 2013A	FY 2014E	FY 2015E	FY 2016E	FY 2017E	FY 2018E	FY 2019E	FY 2020E	FY 2021E	FY 2022E	FY 2023E	FY 2024E	FY 2025E	FY 2026E	FY 2027E	FY 2028E	FY 2029E	FY 2030E	FY 2031E	FY 2032E	FY 2033E
US beloranib PWS sales	0.0	0.0	0.0	0.0	0.0	89.5	157.0	211.4	285.9	293.9	302.1	310.5	319.2	328.1	337.2	346.6	356.2	366.2	376.4	38.7	19.9
US beloranib HIAO sales	0.0	0.0	0.0	0.0	0.0	0.0	74.2	128.8	186.3	251.9	258.9	266.2	273.6	281.2	289.0	297.1	305.3	313.9	322.6	33.2	17.0
Total US beloranib sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**89.5**	**231.2**	**340.2**	**472.2**	**545.8**	**561.0**	**576.7**	**592.7**	**609.2**	**626.2**	**643.7**	**661.6**	**680.0**	**699.0**	**71.8**	**36.9**
EU beloranib PWS sales	0.0	0.0	0.0	0.0	0.0	0.0	88.7	174.9	251.6	338.4	345.9	353.6	361.5	369.5	377.7	386.1	394.7	40.4	20.6	21.1	21.6
EU beloranib HIAO sales	0.0	0.0	0.0	0.0	0.0	0.0	0.0	66.6	130.5	197.2	296.5	303.1	309.8	316.7	323.8	331.0	236.8	34.6	17.7	18.1	18.5
Total EU beloranib sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**88.7**	**241.5**	**382.1**	**535.6**	**642.4**	**656.7**	**671.3**	**686.2**	**701.5**	**717.1**	**631.6**	**74.9**	**38.3**	**39.2**	**40.0**
Total US/EU beloranib sales	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**89.5**	**319.9**	**581.7**	**854.3**	**1081.5**	**1203.5**	**1233.4**	**1264.0**	**1295.5**	**1327.7**	**1360.8**	**1293.1**	**754.9**	**737.3**	**111.0**	**76.9**
Royalties paid to CKD Pharma	0.0	0.0	0.0	0.0	0.0	4.5	16.0	29.1	42.7	54.1	60.2	61.7	63.2	64.8	66.4	68.0	64.7	37.7	36.9	5.5	3.8
Royalties paid to Children's	0.0	0.0	0.0	0.0	0.0	2.7	9.6	17.5	25.6	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 royalties paid	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**7.2**	**25.6**	**46.5**	**68.3**	**54.1**	**60.2**	**61.7**	**63.2**	**64.8**	**66.4**	**68.0**	**64.7**	**37.7**	**36.9**	**5.5**	**3.8**
Total revenue	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**82.4**	**294.3**	**535.1**	**786.0**	**1027.4**	**1143.3**	**1171.7**	**1200.8**	**1230.7**	**1261.3**	**1292.7**	**1228.5**	**717.2**	**700.4**	**105.4**	**73.1**
COGS	**0.0**	**0.0**	**0.0**	**0.0**	**0.0**	**10.7**	**38.4**	**69.8**	**94.0**	**119.0**	**132.4**	**135.7**	**126.4**	**129.5**	**132.8**	**136.1**	**129.3**	**75.5**	**73.7**	**11.1**	**7.7**
R&D	**9.6**	**26.7**	**30.1**	**31.9**	**32.5**	**33.0**	**33.6**	**34.1**	**34.7**	**32.6**	**30.6**	**28.9**	**27.4**	**26.1**	**24.9**	**23.9**	**23.0**	**22.2**	**21.5**	**21.0**	**20.5**
SG&A	**4.2**	**7.2**	**9.8**	**10.1**	**10.3**	**37.5**	**43.7**	**45.4**	**47.1**	**47.8**	**48.6**	**49.3**	**50.1**	**50.9**	**51.7**	**51.4**	**51.2**	**42.7**	**40.5**	**38.6**	**36.9**
Total Operating Expenses	**13.8**	**33.9**	**39.9**	**42.0**	**42.8**	**81.2**	**115.7**	**149.3**	**175.8**	**199.4**	**211.6**	**213.9**	**203.9**	**206.5**	**209.3**	**211.3**	**203.5**	**140.4**	**135.8**	**70.7**	**65.1**
Operating Income (loss)	**(13.8)**	**(33.9)**	**(39.9)**	**(42.0)**	**(42.8)**	**1.2**	**178.6**	**385.9**	**610.1**	**828.0**	**931.7**	**957.8**	**996.9**	**1024.2**	**1052.0**	**1081.4**	**1025.0**	**576.8**	**564.6**	**34.8**	**8.0**
Total other expenses, net	(0.2)	(1.0)	(1.9)	(3.3)	(3.8)	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	0.0
Net loss and comprehensive loss	(14.0)	(34.9)	(40.4)	(45.3)	(46.6)	1.2	178.6	385.9	610.1	828.0	931.7	957.8	996.9	1024.2	1052.0	1081.4	1025.0	576.8	564.6	34.8	8.0
Accretion of redeemable convertible stock	(0.2)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)
Pretax income	(14.2)	(35.1)	(40.5)	(45.4)	(46.7)	1.1	178.5	385.8	610.0	827.9	931.6	957.7	996.8	1024.1	1051.9	1081.3	1024.9	576.7	564.5	34.6	7.9
Income tax expense	0.0	0.0	0.0	0.0	(7.0)	0.2	30.3	123.4	213.5	289.8	326.1	335.2	348.9	358.4	368.2	378.5	358.7	201.8	197.6	6.9	1.6
Tax rate	*0%*	*0%*	*0%*	*0%*	*15%*	*15%*	*17%*	*32%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*20%*	*20%*
Net income (loss)	**(14.2)**	**(35.1)**	**(40.5)**	**(45.4)**	**(39.7)**	**0.9**	**148.2**	**262.3**	**396.5**	**538.1**	**605.5**	**622.5**	**647.9**	**665.7**	**683.7**	**702.8**	**666.2**	**374.8**	**366.9**	**27.7**	**6.3**
GAAP EPS																					
Basic	($19.53)	($2.90)	($1.55)	($1.45)	($1.23)	$0.03	$4.33	$7.44	$10.92	$14.39	$15.72	$15.69	$15.85	$15.81	$15.77	$15.74	$14.48	$7.91	$7.52	$0.55	$0.12
Diluted	($19.53)	($2.90)	($1.55)	($1.45)	($1.23)	$0.03	$4.09	$7.04	$10.33	$13.61	$14.86	$14.83	$14.99	$14.95	$14.91	$14.88	$13.69	$7.48	$7.11	$0.52	$0.12
Basic shares	0.7	12.1	26.2	31.3	32.3	33.2	34.2	35.3	36.3	37.4	38.5	39.7	40.9	42.1	43.4	44.7	46.0	47.4	48.8	50.3	51.8
Diluted shares	0.7	18.6	27.9	33.1	34.1	35.1	36.2	37.3	38.4	39.6	40.7	42.0	43.2	44.5	45.9	47.2	48.6	50.1	51.6	53.2	54.8

Source: SEC filings, RBC Capital Markets estimates

Exhibit 29: Zafgen balance sheet ($MM)

($MM)	FY 2014E	FY 2015E	FY 2016E	FY 2017E	FY 2018E
Cash and cash equivalents	105.6	175.2	366.7	329.0	333.0
Prepaid expenses	0.2	0.2	0.2	0.2	0.2
Tax incentive receivable	1.3	1.0	0.8	0.7	0.5
Total Current Assets	**107.2**	**176.4**	**367.8**	**329.9**	**333.8**
Property and equipment, net	0.0	0.0	0.0	0.0	0.0
Tax incentive receivable	0.0	0.0	0.0	0.0	0.0
Deferred offering costs	0.0	0.0	0.0	0.0	0.0
Total Assets	**107.2**	**176.5**	**367.8**	**330.0**	**333.8**
Accounts payable	2.1	2.2	2.3	2.4	2.6
Accrued expense	0.9	1.0	1.0	1.0	1.0
Total Current Liabilities	**3.0**	**3.2**	**3.3**	**3.5**	**3.6**
Total Liabilities	**3.0**	**3.2**	**3.3**	**3.5**	**3.6**
Redeemable convertible preferred stock	103.8	103.8	103.8	103.8	103.8
Common stock	0.0	0.0	0.0	0.0	0.0
Additional paid-in capital	104.3	214.0	450.6	452.3	455.1
Accumulated deficit	(104.0)	(144.5)	(189.9)	(229.6)	(228.7)
Total Shareholders' Equity	**104.2**	**173.3**	**364.5**	**326.5**	**330.2**
Total Liabilities and Shareholders' Equity	**107.2**	**176.5**	**367.8**	**330.0**	**333.8**

Source: SEC Filings, RBC Capital Markets estimates

Beloranib PWS revenue model

The prevalence estimates of PWS vary, ranging from 1 in 10,000 to 1 in 30,000. We consider 1 in 15,000 as a consensus estimate and use it in our model. This prevalence estimate results in about 21,000 and 34,000 PWS patients in the US and EU, respectively. We also assume that only 35% of PWS patients are correctly identified and that beloranib will be used for patients at least 12-years old. Based on those assumptions, we estimate that the size of addressable patient population for beloranib is around 3,700 and 6,000 initially in the US and EU, respectively. These numbers may increase due to increased physician awareness or expansion of the beloranib label into younger PWS patients.

Net pricing, penetration rates, and sales

In our initial price estimate for beloranib, we assume it would be $156,000/year in the US. In the EU market, we assume it would be $137,000 after taking a 12% discount.

Penetration rate in the US and EU: In our model, we estimate that beloranib's peak penetration rates in the US and EU for PWS to be 50% each. Beloranib could reach US and EU sales in PWS of $632MM in 2022 and peak sales of $751MM in 2029.

Beloranib HIAO revenue model

We will only focus on craniopharyngiomas that develop into HIAO cases, because it represents approximately 90% of HIAO cases and there is more reliable epidemiology data surrounding craniopharyngiomas. The prevalence estimates of HIAO is around 2/100,000, which leads to our estimate of 6,300 and 10,000 patients in the US and EU, respectively. Based on literature reports, we also estimate that 50% of HIAO patients will develop obesity and require drug treatment. Based on these assumptions, we estimate that the size of addressable HIAO patient population for beloranib is around 3,200 and 5,100 initially in the US and EU, respectively.

Net pricing, penetration rates, and sales

We assume that treatment regimen of beloranib for HIAO is the same as it is for PWS. Therefore, the treatment cost would be same between HIAO and PWS.

Penetration rate in the US and EU: In our model, we estimate that beloranib's peak penetration rates in the US and EU for HIAO to be 50% each. Beloranib could reach US and EU sales in HIAO of $449MM in 2022 and peak sales of $628MM in 2028.

Exhibit 30: Beloranib PWS revenue model ($MM) – US

Beloranib PWS Revenue Model ($MM)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
US Beloranib PWS Revenue Model																			
US population	321,347,572	323,821,948	326,315,378	328,828,006	331,359,982	333,911,453	336,482,572	339,073,487	341,684,353	344,315,323	346,966,551	349,638,193	352,330,407	355,043,351	357,777,185	360,532,070	363,308,166	366,105,639	368,924,653
Population growth	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*
PWS prevalence	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*
# of estimated PWS cases	21,423	21,588	21,754	21,922	22,091	22,261	22,432	22,605	22,779	22,954	23,131	23,309	23,489	23,670	23,852	24,035	24,221	24,407	24,595
% of PWS cases that have been identified	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
# of identified PWS cases	7,498	7,556	7,614	7,673	7,732	7,791	7,851	7,912	7,973	8,034	8,096	8,158	8,221	8,284	8,348	8,412	8,477	8,542	8,608
% of PWS patients ≥12 years old	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of PWS patients ≥12 years old	3,749	3,778	3,807	3,836	3,866	3,896	3,926	3,956	3,986	4,017	4,048	4,079	4,111	4,142	4,174	4,206	4,239	4,271	4,304
Beloranib penetration	*0%*	*0%*	*0%*	*17%*	*29%*	*38%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*5%*	*3%*
# of PWS patients treated with beloranib	0	0	0	652	1,121	1,480	1,963	1,978	1,993	2,009	2,024	2,040	2,055	2,071	2,087	2,103	2,119	214	108
Annual revenue/patient				$137,280	$140,026	$142,826	$145,683	$148,596	$151,568	$154,600	$157,692	$160,845	$164,062	$167,344	$170,690	$174,104	$177,586	$181,138	$184,761
Total US beloranib sales in PWS ($MM)			**$0**	**$90**	**$157**	**$211**	**$286**	**$294**	**$302**	**$311**	**$319**	**$328**	**$337**	**$347**	**$356**	**$366**	**$376**	**$39**	**$20**

Source: RBC Capital Markets estimates

Exhibit 31: Beloranib PWS revenue model ($MM) – EU

EU Beloranib PWS Revenue Model	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
EU population	512,559,969	513,687,601	514,817,713	515,950,312	517,085,403	518,222,991	519,363,081	520,505,680	521,650,793	522,798,424	523,948,581	525,101,268	526,256,491	527,414,255	528,574,566	529,737,430	530,902,853	532,070,839	533,241,395
Population growth	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*
PWS prevalence	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*	*0.000067*
# of estimated PWS cases	34,171	34,246	34,321	34,397	34,472	34,548	34,624	34,700	34,777	34,853	34,930	35,007	35,084	35,161	35,238	35,316	35,394	35,471	35,549
% of PWS cases that have been identified	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*	*35%*
# of identified PWS cases	11,960	11,986	12,012	12,039	12,065	12,092	12,118	12,145	12,172	12,199	12,225	12,252	12,279	12,306	12,333	12,361	12,388	12,415	12,442
% of PWS patients ≥12 years old	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of PWS patients ≥12 years old	5,980	5,993	6,006	6,019	6,033	6,046	6,059	6,073	6,086	6,099	6,113	6,126	6,140	6,153	6,167	6,180	6,194	6,207	6,221
Beloranib penetration	*0%*	*0%*	*0%*	*0%*	*14%*	*27%*	*38%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*5%*	*3%*	*3%*	*3%*
# of PWS patients treated with beloranib	0	0	0	0	845	1,632	2,303	3,036	3,043	3,050	3,056	3,063	3,070	3,077	3,083	309	155	155	156
Annual revenue/patient					$105,019	$107,120	$109,262	$111,447	$113,676	$115,950	$118,269	$120,634	$123,047	$125,508	$128,018	$130,578	$133,190	$135,854	$138,571
Total EU beloranib sales in PWS ($MM)				**$0**	**$89**	**$175**	**$252**	**$338**	**$346**	**$354**	**$361**	**$370**	**$378**	**$386**	**$395**	**$40**	**$21**	**$21**	**$22**
Total WW beloranib sales in PWS ($MM)			**$0**	**$90**	**$246**	**$386**	**$538**	**$632**	**$648**	**$664**	**$681**	**$698**	**$715**	**$733**	**$751**	**$407**	**$397**	**$60**	**$41**

Source: RBC Capital Markets estimates

Exhibit 32: Beloranib HIAO revenue model ($MM) – US

Beloranib HIAO Revenue Model ($MM)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
US Beloranib HIAO Revenue Model																			
US population	321,347,572	323,821,948	326,315,378	328,828,006	331,359,982	333,911,453	336,482,572	339,073,487	341,684,353	344,315,323	346,966,551	349,638,193	352,330,407	355,043,351	357,777,185	360,532,070	363,308,166	366,105,639	368,924,653
Population growth	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*	*0.77%*
craniopharyngioma prevalence	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*
# of estimated craniopharyngioma patients	6,427	6,476	6,526	6,577	6,627	6,678	6,730	6,781	6,834	6,886	6,939	6,993	7,047	7,101	7,156	7,211	7,266	7,322	7,378
% of craniopharyngioma cases who develop obesity (HIAO)	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of HIAO patients	3,213	3,238	3,263	3,288	3,314	3,339	3,365	3,391	3,417	3,443	3,470	3,496	3,523	3,550	3,578	3,605	3,633	3,661	3,689
Beloranib penetration	*0%*	*0%*	*0%*	*0%*	*16%*	*27%*	*38%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*5%*	*3%*
# of HIAO patients treated with beloranib	0	0	0	0	530	902	1,279	1,695	1,708	1,722	1,735	1,748	1,762	1,775	1,789	1,803	1,817	183	92
Annual revenue/patient					$137,280	$140,026	$142,826	$145,683	$148,596	$151,568	$154,600	$157,692	$160,845	$164,062	$167,344	$170,690	$174,104	$177,586	$181,138	$184,761
Total US beloranib sales in HIAO ($MM)			**$0**	**$0**	**$74**	**$129**	**$186**	**$252**	**$259**	**$266**	**$274**	**$281**	**$289**	**$297**	**$305**	**$314**	**$323**	**$33**	**$17**

Source: RBC Capital Markets estimates

Exhibit 33: Beloranib HIAO revenue model ($MM) – EU

EU Beloranib HIAO Revenue Model	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E
EU population	512,559,969	513,687,601	514,817,713	515,950,312	517,085,403	518,222,991	519,363,081	520,505,680	521,650,793	522,798,424	523,948,581	525,101,268	526,256,491	527,414,255	528,574,566	529,737,430	530,902,853	532,070,839	533,241,395
Population growth	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*	*0.22%*
craniopharyngioma prevalence	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*	*0.00002*
# of estimated craniopharyngioma patients	10,251	10,274	10,296	10,319	10,342	10,364	10,387	10,410	10,433	10,456	10,479	10,502	10,525	10,548	10,571	10,595	10,618	10,641	10,665
% of craniopharyngioma cases who develop obesity (HIAO)	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*
# of HIAO patients	5,126	5,137	5,148	5,160	5,171	5,182	5,194	5,205	5,217	5,228	5,239	5,251	5,263	5,274	5,286	5,297	5,309	5,321	5,332
Beloranib penetration	*0%*	*0%*	*0%*	*0%*	*0%*	*12%*	*23%*	*34%*	*50%*	*50%*	*50%*	*50%*	*50%*	*50%*	*35%*	*5%*	*3%*	*3%*	*3%*
# of HIAO patients treated with beloranib	0	0	0	0	0	622	1,195	1,770	2,608	2,614	2,620	2,626	2,631	2,637	1,850	265	133	133	133
Annual revenue/patient					$105,019	$107,120	$109,262	$111,447	$113,676	$115,950	$118,269	$120,634	$123,047	$125,508	$128,018	$130,578	$133,190	$135,854	$138,571
Total EU beloranib sales in HIAO ($MM)				**$0**	**$0**	**$67**	**$131**	**$197**	**$296**	**$303**	**$310**	**$317**	**$324**	**$331**	**$237**	**$35**	**$18**	**$18**	**$18**
Total WW beloranib sales in HIAO ($MM)			**$0**	**$0**	**$74**	**$195**	**$317**	**$449**	**$555**	**$569**	**$583**	**$598**	**$613**	**$628**	**$542**	**$348**	**$340**	**$51**	**$36**

Source: RBC Capital Markets estimates

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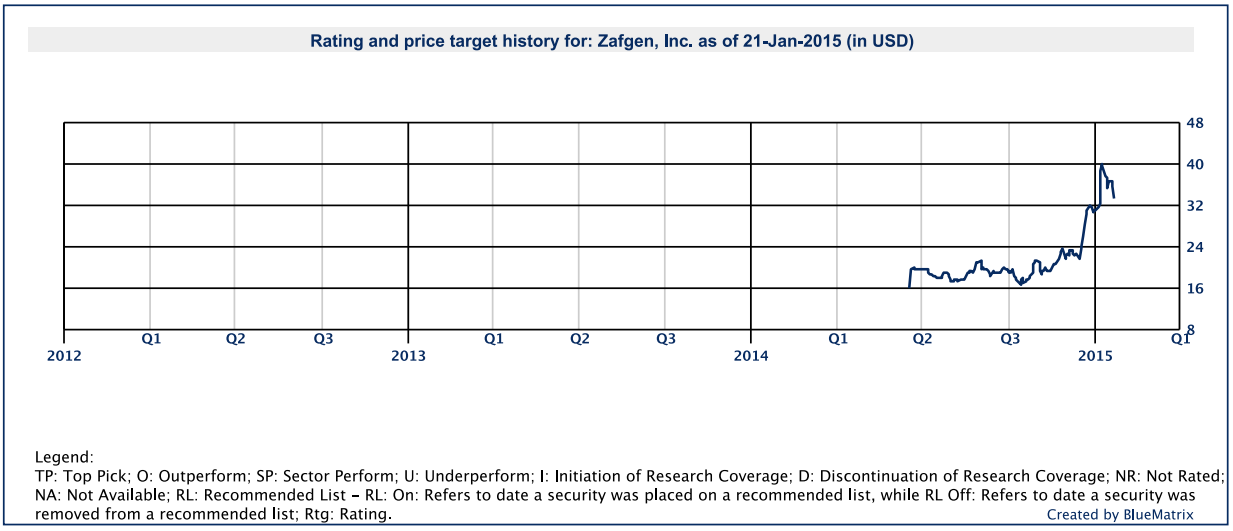

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