Refocusing Resources on ZGN-1061

July 19, 2016

Forward Looking Statements

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Refocusing Resources on ZGN-1061

Suspending development of beloranib following comprehensive review

- Recent FDA Type A meeting to discuss path forward in PWS
- Costs and timelines to commercialization are too great to justify continued investment given other pipeline opportunities

Shifting focus to second-generation MetAP2 inhibitor, ZGN-1061

- Differentiated profile of ZGN-1061 vs. beloranib
- Ideally suited to develop in more prevalent indications such as severe and complicated obesity

Scaling organization to reflect new development priorities

Strong cash position to support ZGN-1061 development

Second-Generation MetAP2 Inhibitor Discovery Overview – Discovery of ZGN-1061

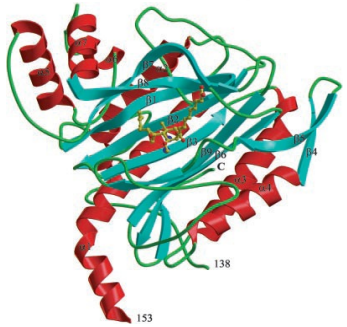
Multiple Chemical Classes

337 analogs designed and tested

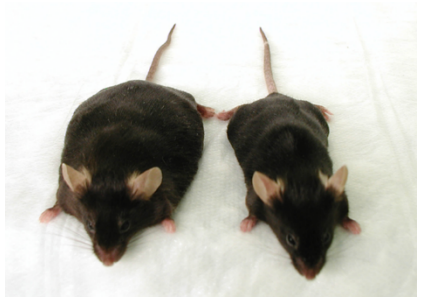
Extensive Profiling of 195 compounds for Optimal Performance in Pharmacological Models

Refined inhibitor collection optimized for:
Efficacy
Safety
Novelty

Potency
- MetAP2
- Counter-Screens
- In vitro profiling



PK/PD
- Weight Loss
- Biomarker Impact
- Physical Properties

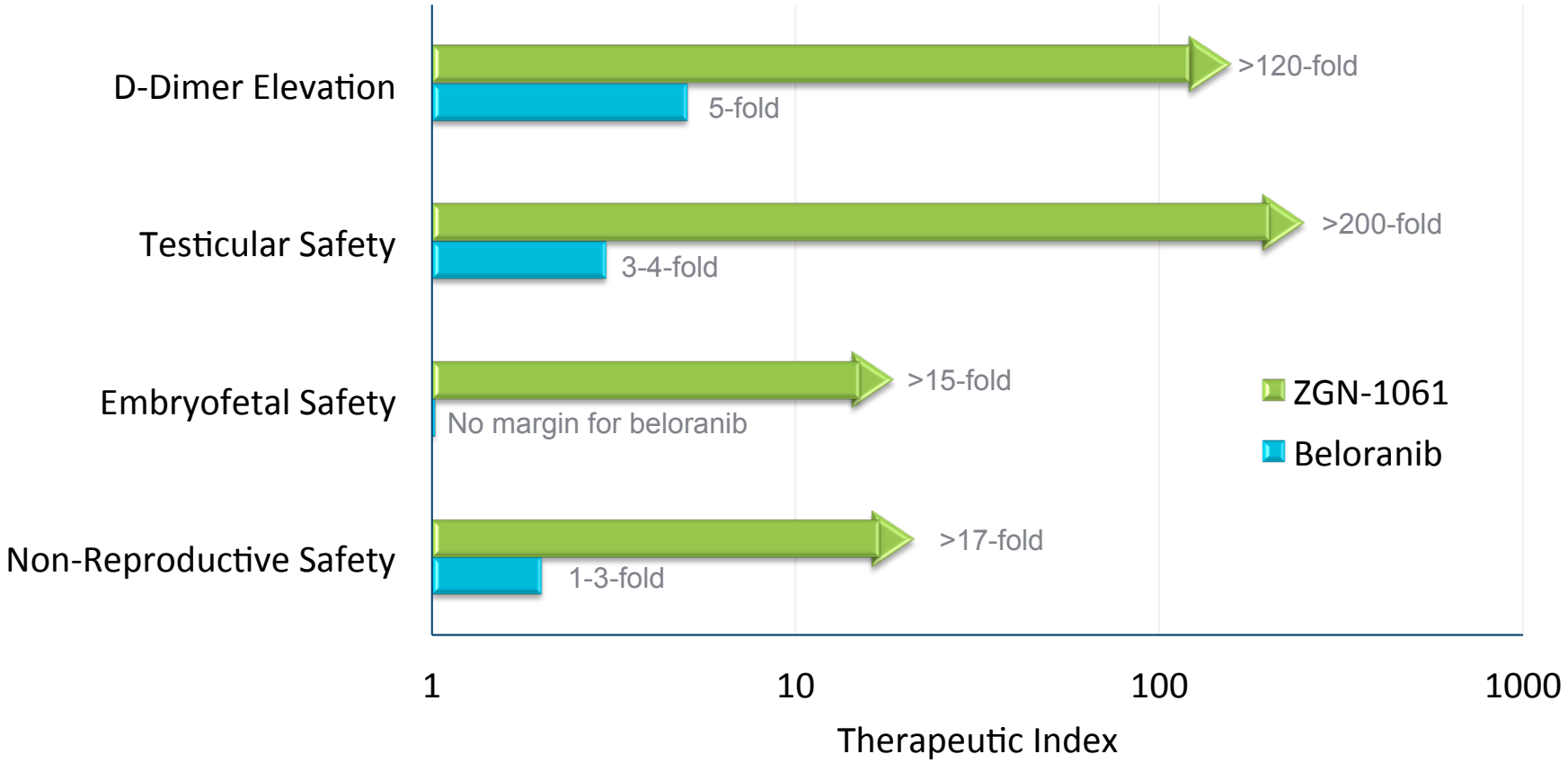


Safety
- Teratology
- Testicular function
- Thrombosis

ZGN-1061: Highly Optimized, More Advanced MetAP2 Inhibitor

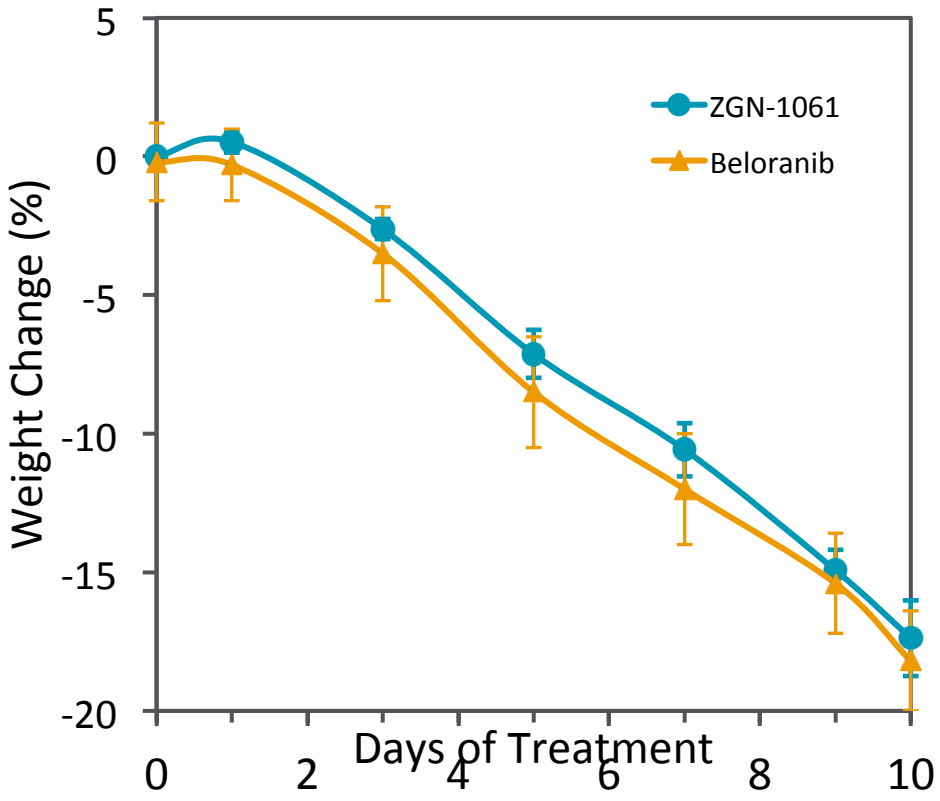
		Beloranib	ZGN-1061
Efficacy	**Impact on weight loss, glycemic control, CV risk factors**	Fully effective based on preclinical and clinical data	Fully effective based on preclinical data
Preclinical Safety	**Embryofetal development impact**	No margin	Substantial margin
	Testicular function impact	Narrow margin	No impact
	Thrombotic risk	Narrow margin	Substantial margin
Economics	**Royalties/milestones due**	Up to $22.5M in milestones; single digit royalties	None; Wholly-owned
	Manufacturing	Complex	Simplified
	Patent life	2029-2031	2036+
Opportunity	**Markets**	Orphan indications	Prevalent metabolic indications
	Lead indication(s)	PWS, HIAO	Severe and Complicated Obesity

ZGN-1061 has been Optimized for Markedly Improved Safety Margins* vs. Beloranib in Non-Clinical Studies



*Values represent the ratio of exposures observed or estimated at no observed adverse effect level (NOAEL) doses from animal studies in which endpoints have been observed, relative to known exposures for beloranib (2.4 mg twice-weekly) or projected effective clinical exposures for ZGN-1061. Ranges represent the lowest and highest estimated ranges based on male and female animals, where relevant, of all species evaluated. Results are from animals and are not necessarily predictive of human results or results of longer-term studies.

ZGN-1061 is Equally Effective as Beloranib in Reducing Body Weight in Obese Mice



ZGN-1061 and beloranib have similar impact on metabolic parameters in preclinical models

- Body weight
- Food intake
- Plasma lipids (TG and Cholesterol)
- Blood glucose
- Liver function tests

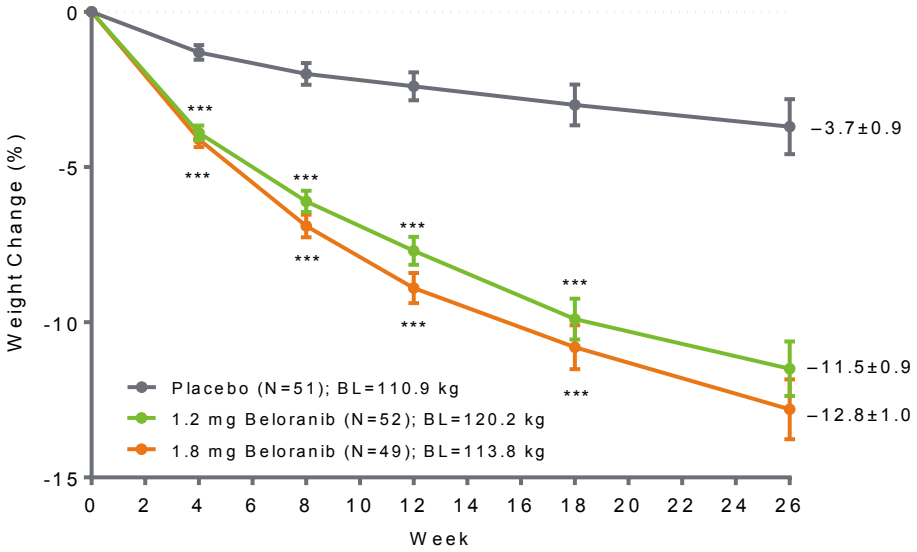
Obese high fat diet-fed C57Bl/6 were treated with ZGN-1061 or beloranib for 10 days by subcutaneous injection at doses leading to similar plasma drug exposures (0.1 mg/kg beloranib vs. 0.3 mg/kg ZGN-1061). Values represent vehicle-adjusted weight change and means ± SEM for n=4 mice per group.

Leveraging Experience with MetAP2i in Obese Patients with Diabetes to Design Efficient Clinical Program for ZGN-1061

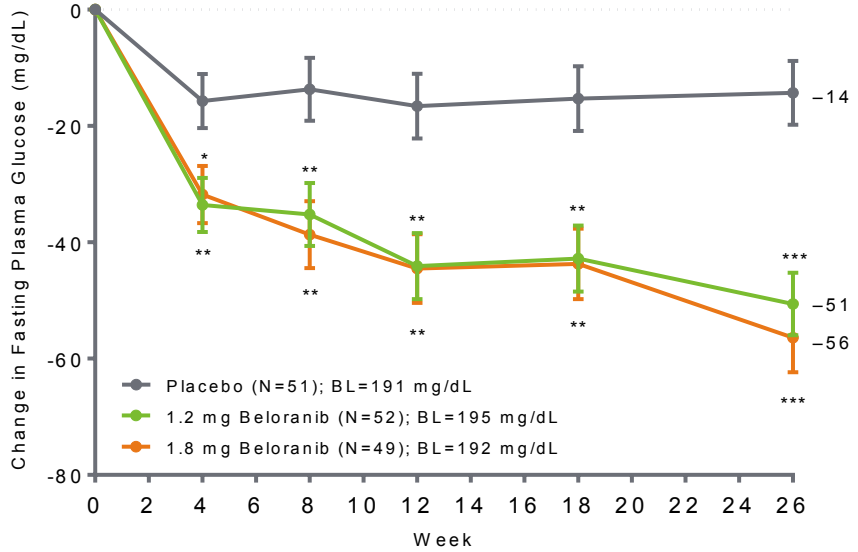
Early, compelling responses observed in ZAF-203 Phase 2b clinical trial

- Body weight loss and glycemic control was evident following 4 weeks of beloranib treatment, and strengthened after 12 weeks of treatment
- 4- and 12-week Phase 1 and 2 clinical trials with ZGN-1061 should be adequate to confirm efficacy in obese and type 2 diabetes patients

Reduction in Body Weight



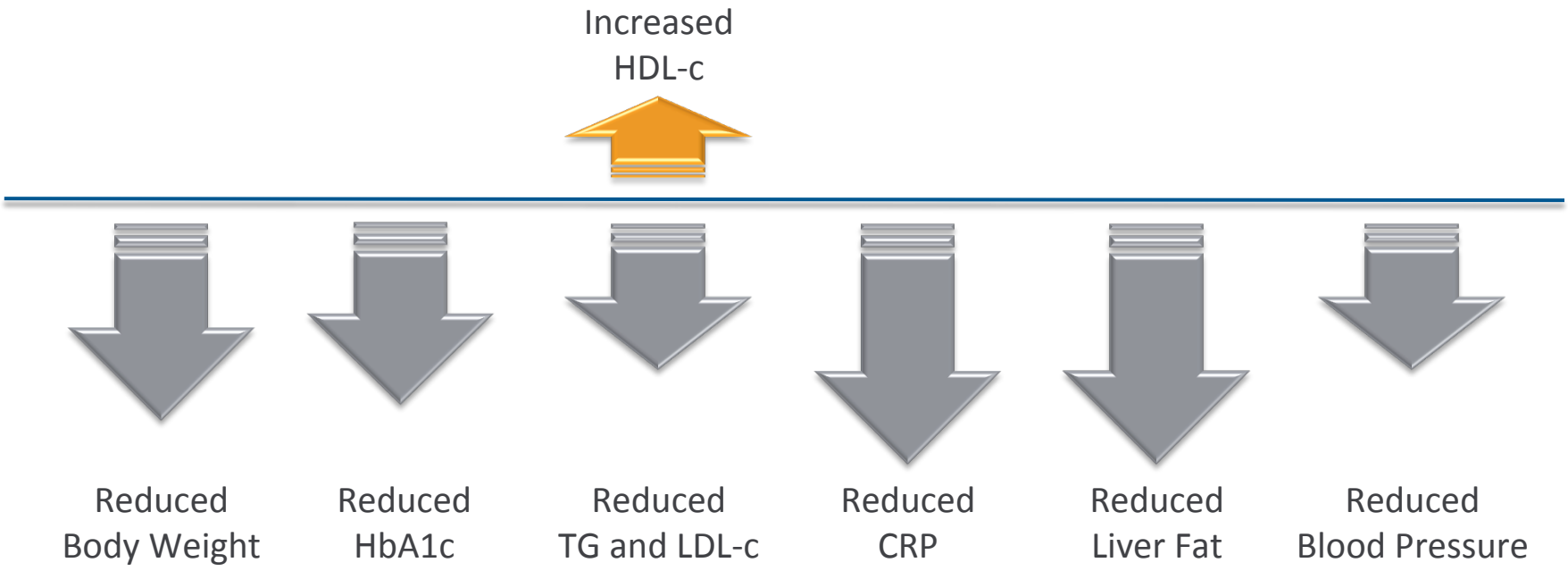
Reduction in Glucose



*p<0.05, **p<0.01, ***p<0.0001 for change from baseline with beloranib vs. placebo

MetAP2i Efficacy Beyond Weight Loss 'Pre-validated' through Beloranib Clinical Trials, Shaping a Vision for ZGN-1061

MetAP2 inhibitor therapy with beloranib improved body weight and glycemic control while reducing cardiovascular disease risk factors



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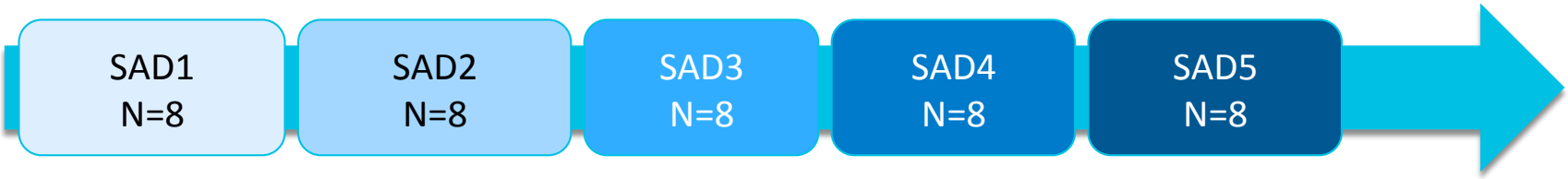
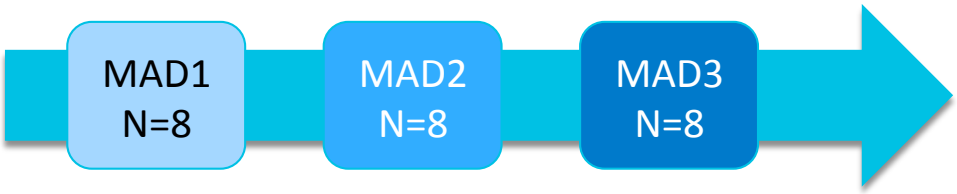
ZGN-1061 Phase 1 Clinical Trial

Part 1: Single Ascending Dose Study



- N=6/2 (active/placebo) per cohort, 5 cohorts
- ~14 day interval between each dose level

Part 2: Multiple Ascending Dose Study



- N=6/2 (active/placebo) per cohort, 3 cohorts
- Twice-weekly SC dosing for 28 days (8 injections)

ZGN-1061 Phase 1 Outcome Measures

Primary

- Evaluate safety and tolerability of ZGN-1061

Secondary

- Characterize and confirm improved pharmacokinetic profile for ZGN-1061

Exploratory

- Study pharmacodynamic endpoints, including body weight, fat mass, waist and hip circumference, food intake, self-reported appetite, lipids, and other blood markers

Key Decision-Driving Endpoints related to PK/Thrombosis

- Drug exposure/PK profile, coagulation biomarkers, thrombotic endpoints

Phase 1 Data Expected by End of Q1 2017

Aligning Operations with New Clinical Focus

Reducing workforce by ~34%, to a total of 31 employees, by December 2016

- Reductions mainly in pre-commercial, clinical, regulatory, G&A
- Expect ~$4.8M in reduced annualized workforce expenses once fully implemented
- Expect to incur a non-recurring charge of ~$2.4 million in 3Q16

Strong cash position to drive development of ZGN-1061 through proof-of-concept

- Cash as of June 30, 2016 of $150.5M
- Expect to end 2016 with >$125M in cash
- Cash sufficient to fund operations through end of 2018
- Resources to support development of ZGN-1061 through Phase 2a clinical trials

Zafgen: The Leader in the Development of MetAP2 Inhibitors

- MetAP2 pathway has demonstrated significant potential in the treatment of severe and complicated obesity
- 1st-generation compound beloranib provided strong validation with clinically meaningful impact on weight loss, glycemic control and CV risk factors
- 2nd-generation candidate ZGN-1061 ideally suited for prevalent obesity indications, including severe and complicated obesity
- Leveraging deep knowledge of MetAP2 inhibition to advance ZGN-1061 with clearly defined development path
- Strong cash position supports development of ZGN-1061 through key inflection points

Q&A

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Thank You

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