zafgen

Zafgen
PWS Clinical Trial
Program Overview

November 16, 2014

Disclaimers

Forward Looking Statements

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as “may,” “might,” “will,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “project,” “intend,” “future,” “potential,” or “continue,” and other similar expressions are intended to identify forward looking statements. For example, all statements we make regarding the initiation, timing, progress and results of our preclinical and clinical studies and our research and development programs, our ability to advance product candidates into, and successfully complete, clinical studies, and the timing or likelihood of regulatory filings and approvals are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. These statements are also subject to a number of material risks and uncertainties that are described in the preliminary prospectus. Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Zafgen Pipeline

Novel Portfolio Leveraging MetAP2 Target in Metabolic Diseases

Drug Candidate	Indication	Preclinical	Phase 1	Phase 2	Phase 3	Next Milestone
Beloranib Fumagillin-class MetAP2i	***Prader-Willi syndrome***	***Twice-weekly subcutaneous (SC) injection***				U.S. Phase 3 results Q4 2015
Beloranib Fumagillin-class MetAP2i	***Hypothalamic injury (HIAO)***	***Twice-weekly (SC) injection***				Complete Phase 2a trial 4Q 2014
Beloranib Fumagillin-class MetAP2i	***Severe obesity***	***Twice-weekly (SC) injection***				Initiate Phase 2b trial 2H 2014
2nd Generation MetAP2i	***General obesity***	***SC Injection***				Candidate Nomination
ZGN-839 Novel chemical class MetAP2i	***NASH / Type 2 diabetes***	***Oral***				IND 1H 2015

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

zafgen

Beloranib

Powerful Small Molecule MetAP2 Inhibitor

Rebalances lipid metabolism & body composition, and reduces hunger

Liver Effects

- Reduces fat and cholesterol synthesis
- Increases ketone body production
- Reduces LDL cholesterol and C-reactive protein

Adipose Tissue Effects

- Increases fat mobilization and use of stored fat as energy source

Hunger Reduction

- Reduces hunger and food intake assisting weight loss and improving behavior - patients lose weight but feel less hungry

Convenience and Control

- Low dose twice-weekly subcutaneous injection

zafgen

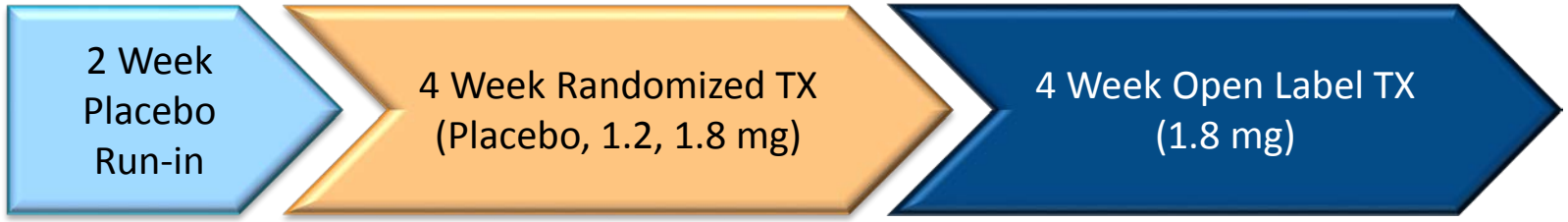
ZAF-211: Proof of Concept Trial

Trial Population

- 17 Patients in group home setting
- Genetically confirmed PWS
- Obese – BMI average ~31 kg/m^2
- 50% Increased food allowance

Key Readouts

- Biomarkers
- Hyperphagia-related behaviors
- Body composition and weight
- Safety and tolerability



n=17 n=6,5,6 n=17

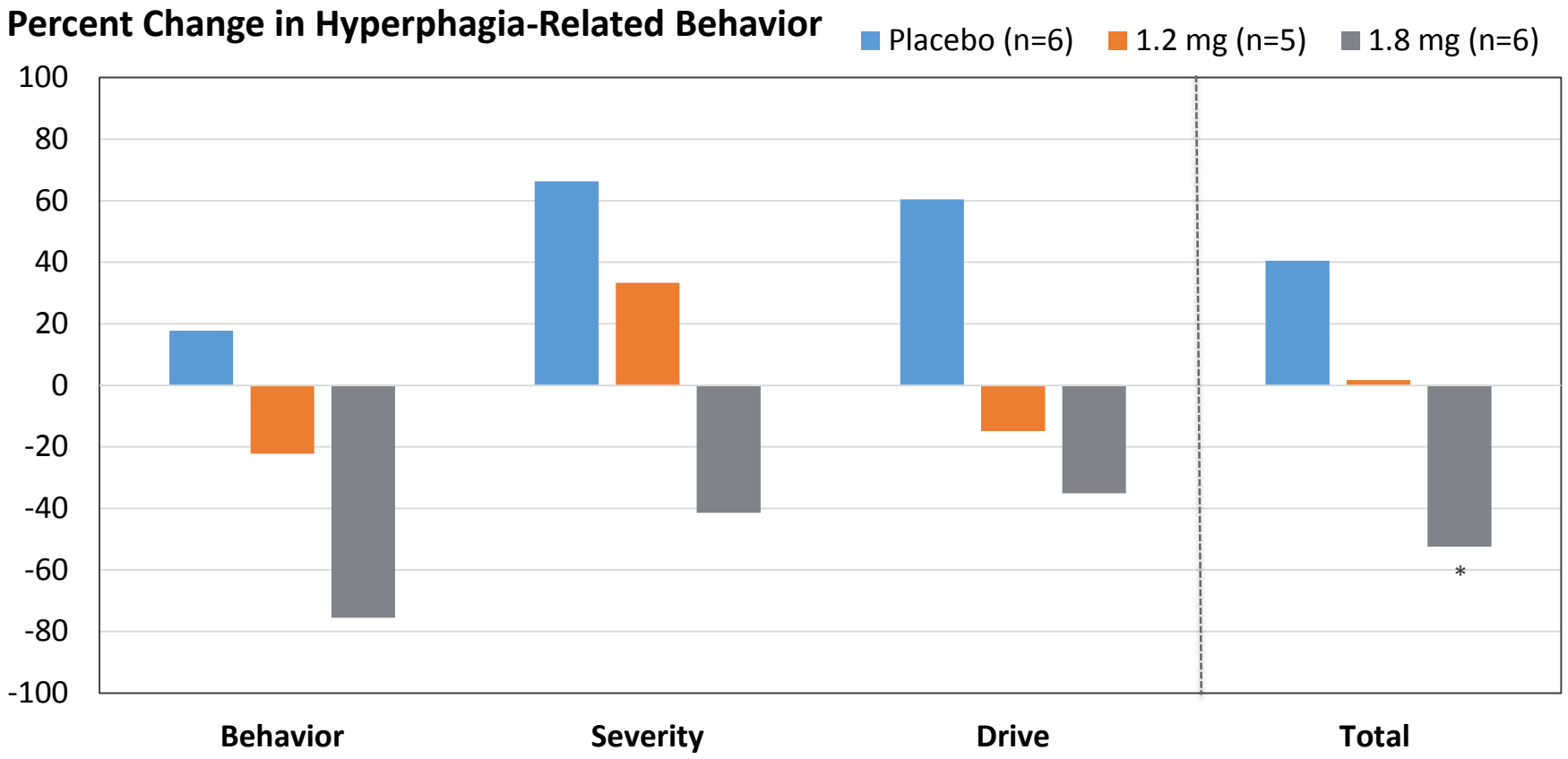
Key Findings

- Well-tolerated – no safety signals
- Clear evidence drug pathway is responsive in PWS patients including LDL-c reduction
- Improved hyperphagia-related behaviors
- Reduced body fat content vs. placebo

} Planned registration endpoints

zafgen

ZAF-211: Hyperphagia Scores Show Dose-Responsive Improvement in Adverse Behaviors

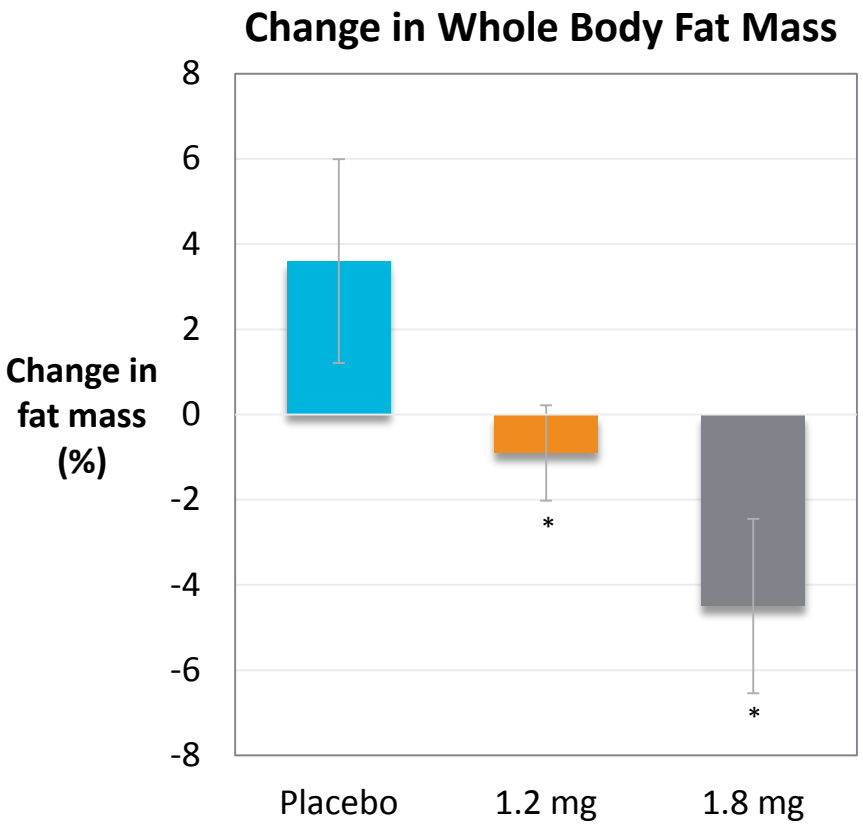


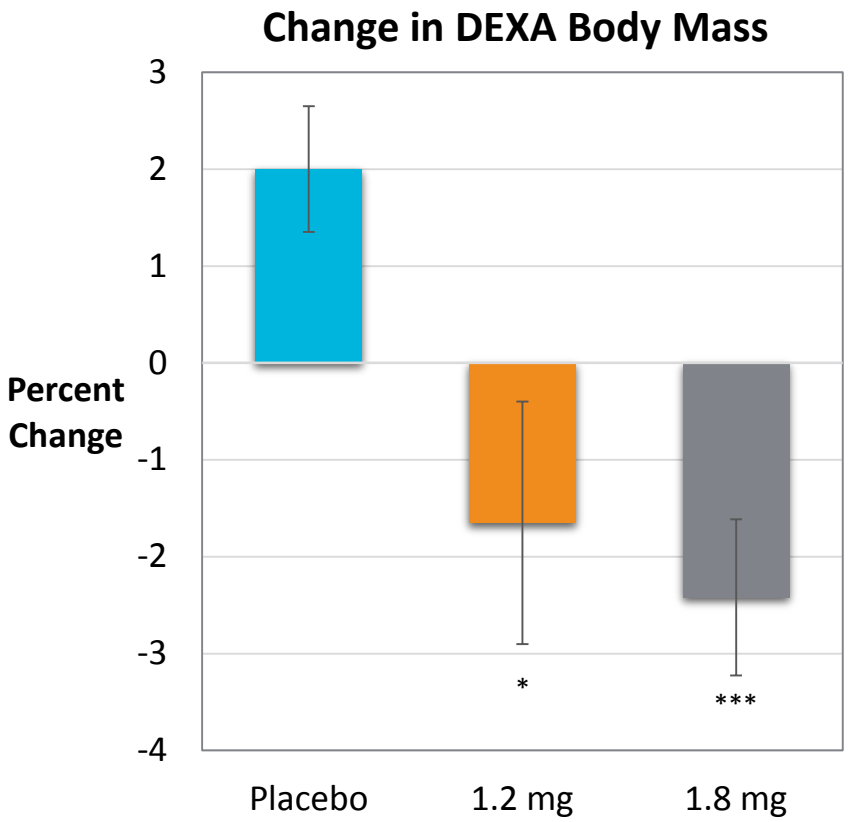
*, p<0.05

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

zafgen

ZAF-211: Fat Mass and Total Body Mass Reduction Despite Increased Caloric Intake





*, p<0.05; ***, p<0.005

Body composition and mass assessed by DEXA, dual-energy X-ray absorptiometry

zafgen

Investigating a New Approach to Combat Disease-Driven Obesity

bestPWS

Beloranib Efficacy, Safety and Tolerability in Prader-Willi Syndrome

bestPWS Trial Summary

- Obese PWS volunteers aged 12-65 years
- Placebo-controlled
- Medication administered by a home health nurse
- Option to receive active study medication during 6-month open-label phase
- Travel costs will be reimbursed

For more information about bestPWS, visit www.clinicaltrials.gov and enter search terms Zafgen PWS or beloranib

Phase 3 Study Overview

- Randomized, double-blind, placebo-controlled
- Parallel dosing groups
- ~14 sites in US
- 84 patients to be randomized to 1 of 4 dosing arms

Enrollment and randomization scenario

Dose	# of Pts
2.4 mg	28
1.8 mg	28
Placebo	28
	84

- 6 months randomized treatment
- Completers of randomized treatment have option to enroll in open-label treatment extension for another 6 months (separate protocol ZAF-311E)

Study Objectives

Primary

- Assess change in hyperphagia related behavior as measured by the Dykens hyperphagia questionnaire and total body fat mass as measured by dual X-ray absorptiometry (DEXA)
- Assess safety and tolerability

Secondary

- Assess change in body weight and metabolic parameters
- Assess Quality of Life (QoL) impact for patients and caregivers

Study Population

- Patients with Prader-Willi syndrome (genetically confirmed)

  Patients living in group homes (≥ 50% of time) will be excluded
- Males and females
- BMI ≥30 and ≤60 kg/m^2 for adults or BMI ≥95th percentile for adolescents (based on age and gender)
- Age 12-65
- Patients with type 2 diabetes allowed
  - HbA1c <10%, FPG <240 mg/dL
  - Not on insulin - if on GLP-1, must have been stable for 6 months

Study Population

- Hyperphagia total score ≥13 (scale of 0-36)
- Patient needs to have at least 1 consistent and reliable primary caregiver
  - Spends at least 4 waking hrs/day on average with patient
  - Has been caring for patient for at least 6 mons
  - Remain caring for patient for duration of study

  Caregivers will assess changes in patient's hyperphagia related behavior, quality of life, maladaptive behavior, AEs, etc. throughout study
- Patient needs to have at least one consistent and reliable caregiver or chaperone for site visits
- Caregiver must be able to understand and read English

zafgen

Thank you