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

<table>
<thead>
<tr>
<th>Drug Candidate</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Next Milestone</th>
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<tbody>
<tr>
<td>Beloranib Fumagillin-class MetAP2i</td>
<td>Prader-Willi syndrome</td>
<td></td>
<td><em>Twice-weekly subcutaneous (SC) injection</em></td>
<td></td>
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<td>U.S. Phase 3 results Q4 2015</td>
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<tr>
<td>Beloranib Fumagillin-class MetAP2i</td>
<td>Hypothalamic injury (HIAO)</td>
<td><em>Twice-weekly (SC) injection</em></td>
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<td>Complete Phase 2a trial 4Q 2014</td>
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<tr>
<td>Beloranib Fumagillin-class MetAP2i</td>
<td>Severe obesity</td>
<td><em>Twice-weekly (SC) injection</em></td>
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<td>Initiate Phase 2b trial 2H 2014</td>
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<tr>
<td>2nd Generation MetAP2i</td>
<td>General obesity</td>
<td><em>SC Injection</em></td>
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<td>Candidate Nomination</td>
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<td>ZGN-839 Novel chemical class MetAP2i</td>
<td>NASH / Type 2 diabetes</td>
<td><em>Oral</em></td>
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<td>IND 1H 2015</td>
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Zafgen owns world-wide commercial rights to all compounds (exclusive of Korea for beloranib)
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
ZAF-211: Proof of Concept Trial

**Trial Population**
- 17 Patients in group home setting
- Genetically confirmed PWS
- Obese – BMI average ~31 kg/m²
- 50% Increased food allowance

**Key Readouts**
- Biomarkers
- Hyperphagia-related behaviors
- Body composition and weight
- Safety and tolerability

**Trial Timeline**
- 2 Week Placebo Run-in (n=17)
- 4 Week Randomized TX (Placebo, 1.2, 1.8 mg) (n=6,5,6)
- 4 Week Open Label TX (1.8 mg) (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
ZAF-211: Hyperphagia Scores Show Dose-Responsive Improvement in Adverse Behaviors

Reduction in behavior sub-scores were seen from baseline following randomized treatment with 1.8 mg beloranib
ZAF-211: Fat Mass and Total Body Mass Reduction Despite Increased Caloric Intake

**Change in Whole Body Fat Mass**

- Placebo
- 1.2 mg
- 1.8 mg

**Change in DEXA Body Mass**

- Placebo
- 1.2 mg
- 1.8 mg

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

Body composition and mass assessed by DEXA, dual-energy X-ray absorptiometry
Investigating a New Approach to Combat Disease-Driven Obesity

bestPWS

Beloranib Efficacy, Safety and Tolerability in Prader-Willi Syndrome
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

<table>
<thead>
<tr>
<th>Dose</th>
<th># of Pts</th>
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<tr>
<td>2.4 mg</td>
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<tr>
<td>1.8 mg</td>
<td>28</td>
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<tr>
<td>Placebo</td>
<td>28</td>
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<tr>
<td></td>
<td>84</td>
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Enrollment and randomization scenario

- 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/m² 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 $\geq 13$ (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