zafgen

Second Quarter 2017 Financial Results

August 8, 2017

Agenda

- Tom Hughes – 2Q 2017 Highlights
- Dennis Kim - ZFGN-1061 Clinical Results and Preclinical Data
- Patty Allen - Financials
- Tom Hughes – Conclusion
- Q&A

Disclaimers

Forward Looking Statements

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2Q17 Highlights

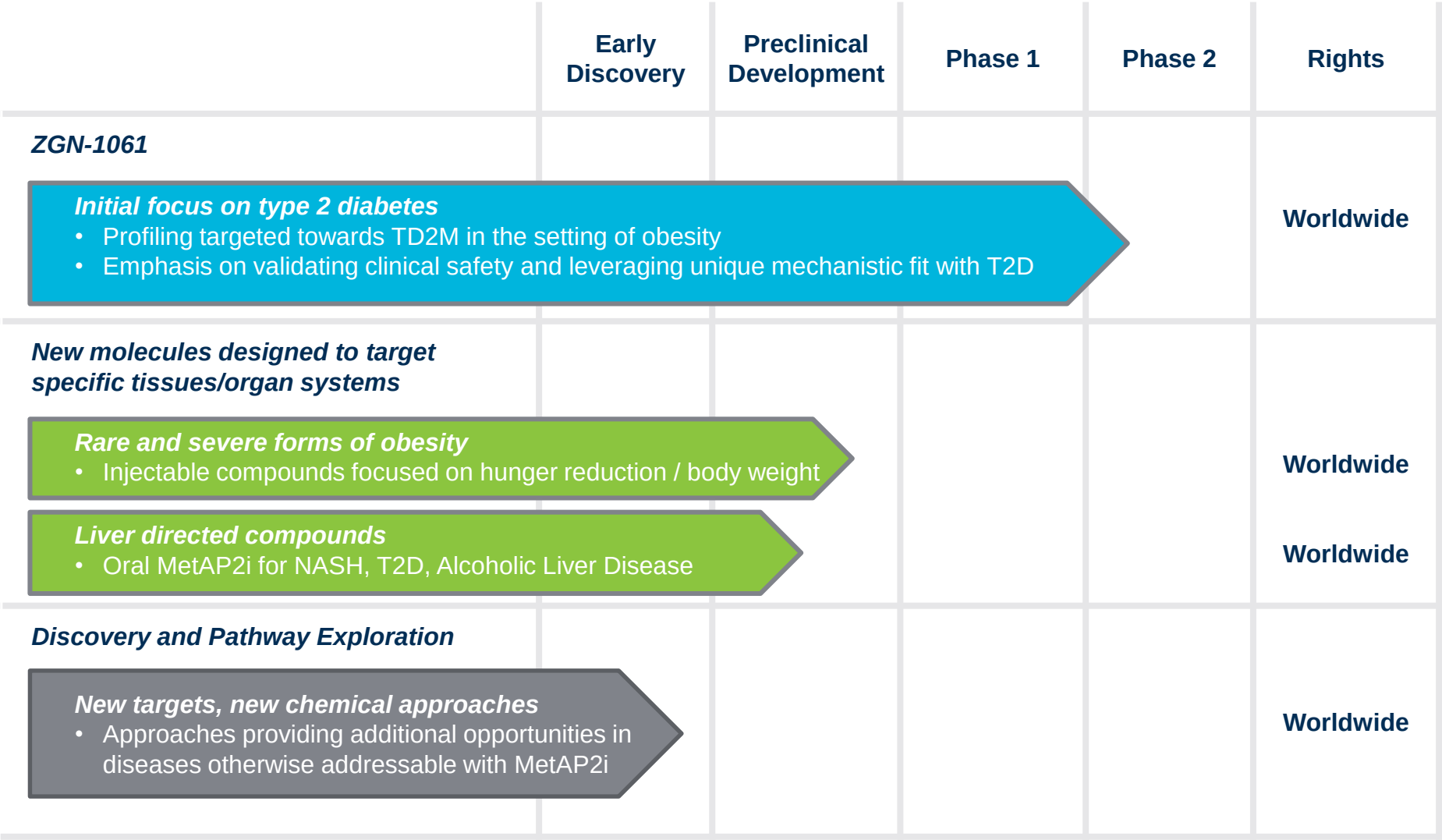
Tom Hughes, Ph.D., President and Chief Executive Officer

Recent Data Highlights Potential of ZGN-1061

- Phase 1 clinical trial showed that it was well-tolerated and safe
- Pharmacokinetic and target engagement profile met our prospectively established criteria
- Weight change supportive of drug effect
- Metabolic parameter changes consistent with MetAP2 inhibitor effects
- Differentiated profile supports development into later-stage development

On track to initiate Phase 2 clinical trial in type 2 diabetes in 3Q 2017

Novel Portfolio Providing Multiple Development Programs Focused on Metabolic Diseases



ZGN-1061 Clinical Update

Dennis Kim, M.D., Chief Medical Officer

ZAF-1061-101 Clinical Trial Design and Demographics

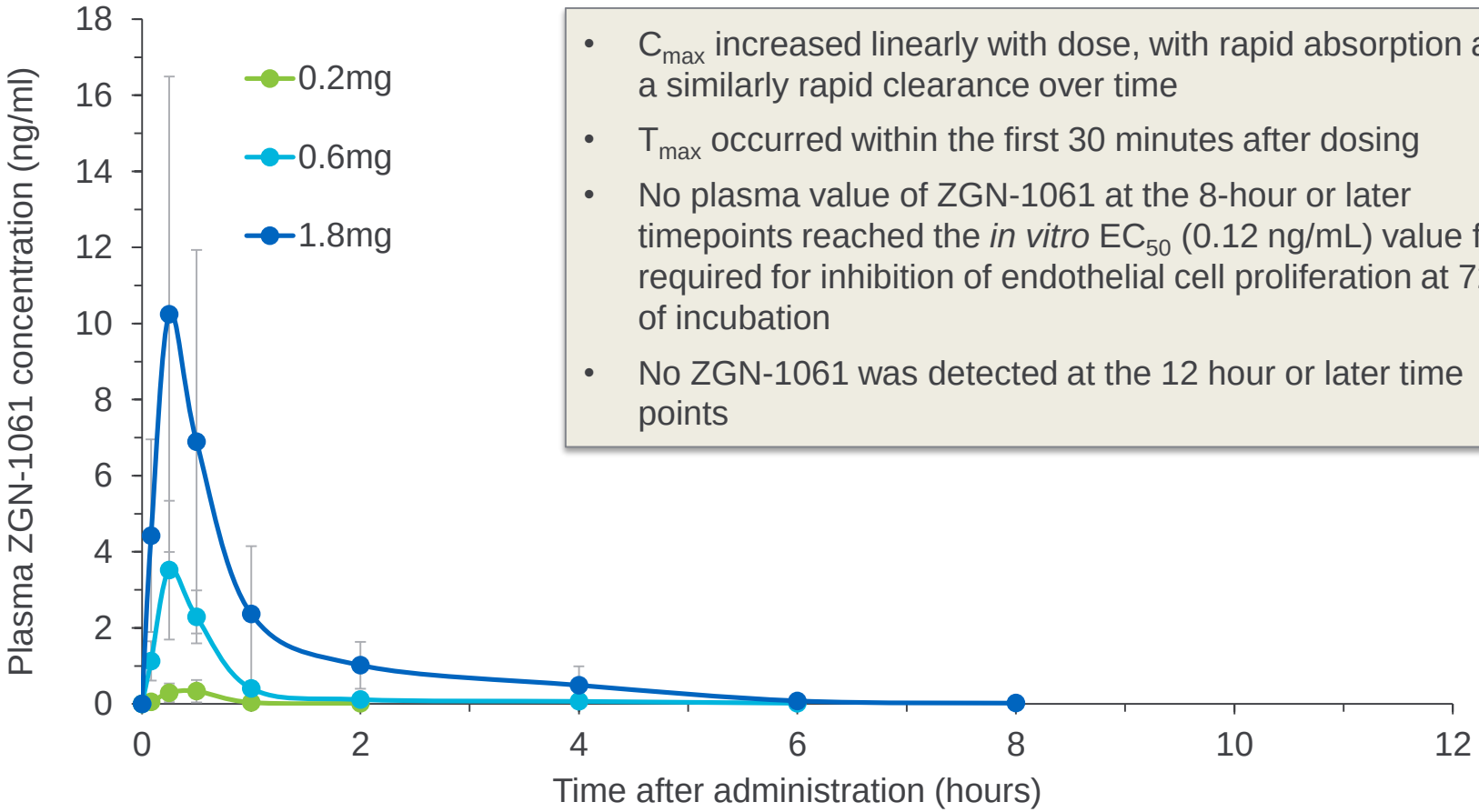
ZAF-1061-101	Single Ascending Dose (SAD)	Multiple Ascending Dose (MAD)
Patient population	Healthy	Healthy, obese
N	39	29
Demographics	90% male; average BMI of 26	76% male; average BMI of 33
Dosing cohorts	0.2, 0.6, 1.2, 2.4, 3.6, 4.8 mg	0.2, 0.6, 1.8 mg
Dosing schedule	Single dose	Twice-weekly dosing for 28 days (8 injections)
Randomization	3:1 (active/placebo)	3:1 (active/placebo)
In-patient treatment	Domiciled days -1 through 4	Domiciled for the majority of the trial for closer safety monitoring: • No exercise allowed • Controlled food intake, including meal challenges

ZAF-1061-101 MAD Phase: Safety Summary

- Safe and well-tolerated
  - No serious adverse events (SAEs), no severe adverse events (AEs)
  - No AEs leading to early withdrawal from the clinical trial
  - All AEs were of mild intensity in the MAD phase except one (toothache)
  - Most common side effects were mild gastrointestinal issues (comparable between ZGN-1061 relative to placebo), headache and procedural related irritation
  - No sleep disturbance

- Reassuring thrombosis-relevant data
  - No venous thromboembolisms (VTEs)
  - No D-dimer elevations indicative of the presence of VTEs
  - No meaningful elevations in mean D-dimer concentrations across the dosing groups compared to baseline or placebo
  - No changes in standard coagulation laboratory values

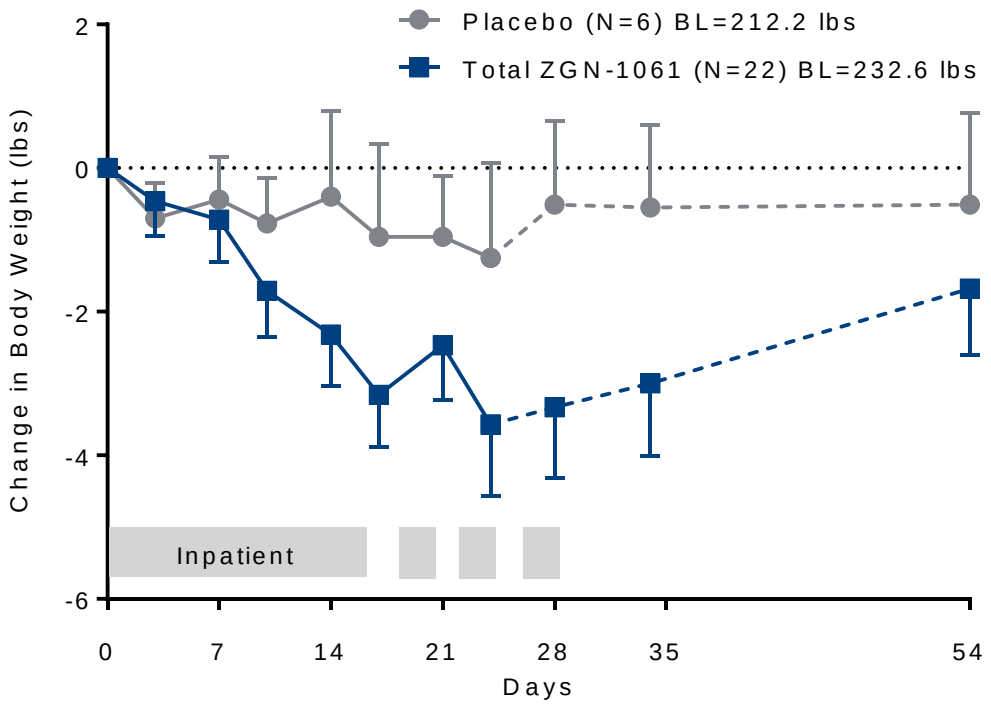
ZGN-1061 Pharmacokinetic Profile Meets Prospectively Established Criteria



- C_{max} increased linearly with dose, with rapid absorption and a similarly rapid clearance over time
- T_{max} occurred within the first 30 minutes after dosing
- No plasma value of ZGN-1061 at the 8-hour or later timepoints reached the *in vitro* EC_{50} (0.12 ng/mL) value for required for inhibition of endothelial cell proliferation at 72h of incubation
- No ZGN-1061 was detected at the 12 hour or later time points

Values are mean ± SD

Body Weight Loss Was Steady and Progressive During ZGN-1061 Treatment with Rebound Post-treatment, Supporting a Drug Effect



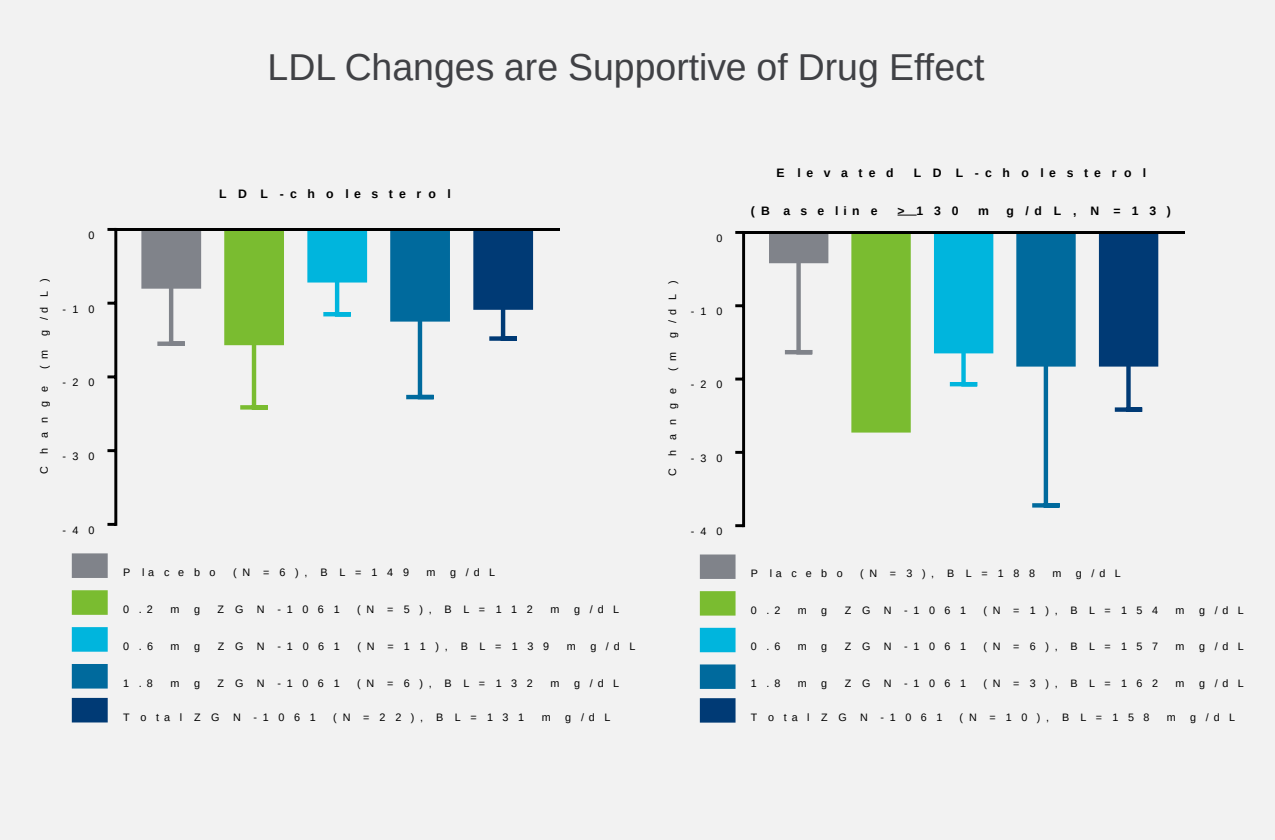
Dashed lines indicate washout period during which no treatments were administered.

- Following discontinuation of treatment, ZGN-1061-treated patients on average experienced weight regain. This is supportive of a drug effect to lower body weight.
- Longer dosing is expected to drive continued weight loss as seen for beloranib

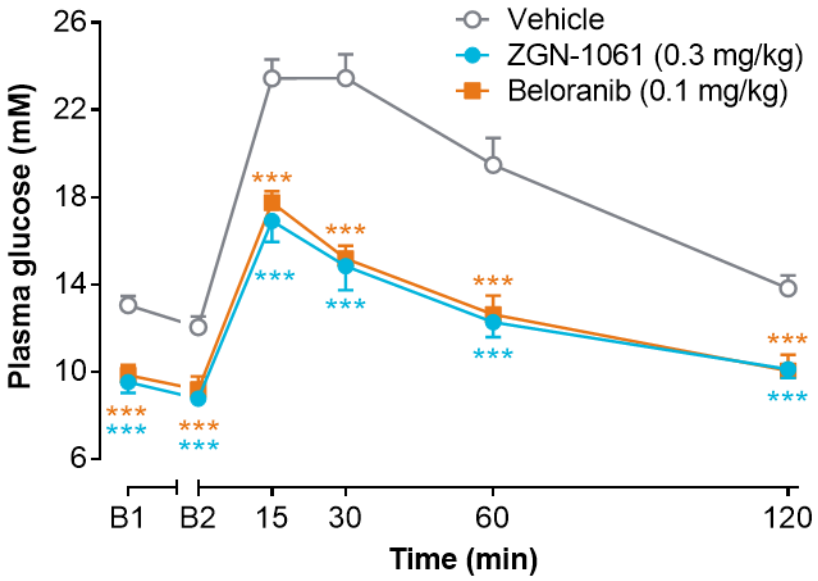
Trends for Improvement Across Multiple Metabolic Measures Supportive of Drug Activity

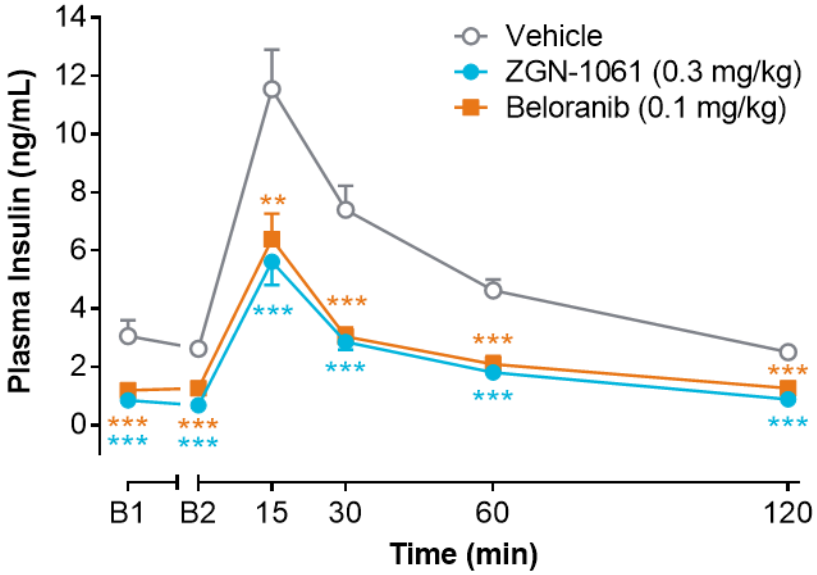
Trends observed in:

- Waist circumference
- Food intake
- C-reactive protein (CRP)
- Adiponectin
- Leptin



ZGN-1061 Shows Comparable Improvement in Glucose Tolerance as Beloranib in DIO Mice

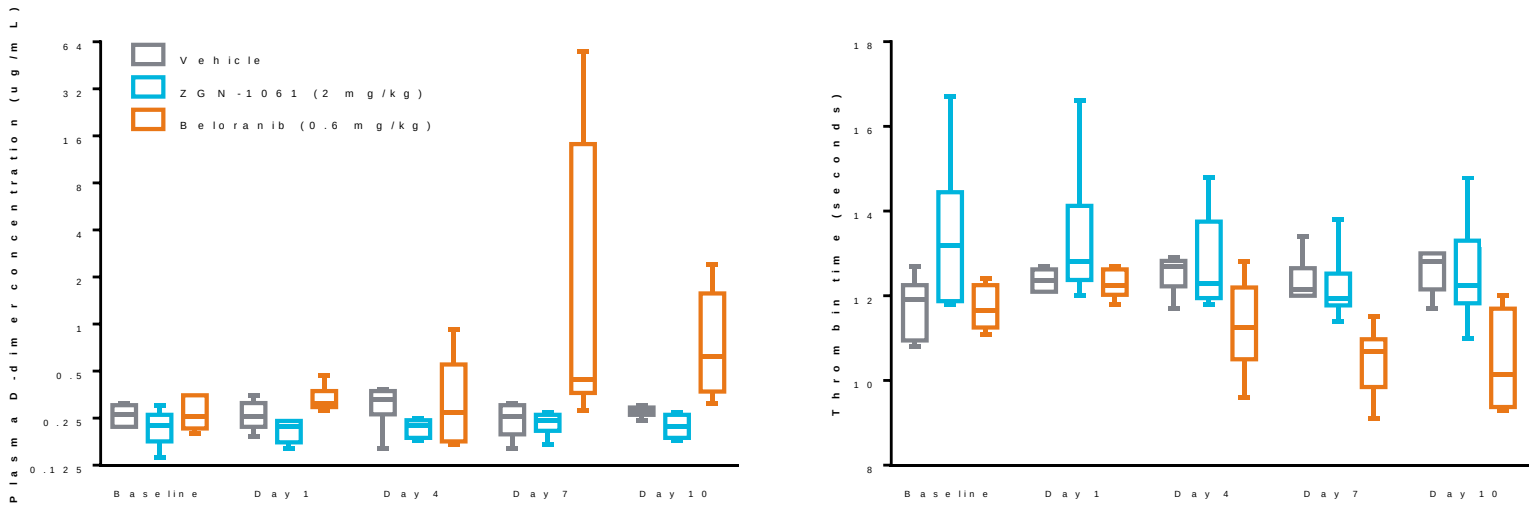




Data are mean and SEM. Mice (n=9−10/group) were fasted overnight and dosed with vehicle or study drug SC. An oral glucose tolerance test was performed 60 minutes after dosing (t =0 min). Blood samples were obtained at t =−60 min (B1), 0 min (B2), and 15, 30, 60, and 120 min. Data are calculated from the residuals of the statistical models. Comparisons vs Vehicle of treatments were by Williams' test (ZGN-1061) and multiple t-test (beloranib). **p<0.01 and ***p<0.001 vs Vehicle. Abbreviations: SEM = standard error of the mean.

ZGN-1061: Improved Safety Profile for Markers of Thrombosis Compared to Beloranib

- ZGN-1061 does not affect thrombosis markers that are changed by beloranib in endothelial cells after up to 8 hours of exposure, including P21, thrombomodulin and PAI-1
- In contrast to beloranib, which produced changes in the coagulation markers D-dimer and thrombin time at 0.6 mg/kg, ZGN-1061 had no effect at 2 mg/kg



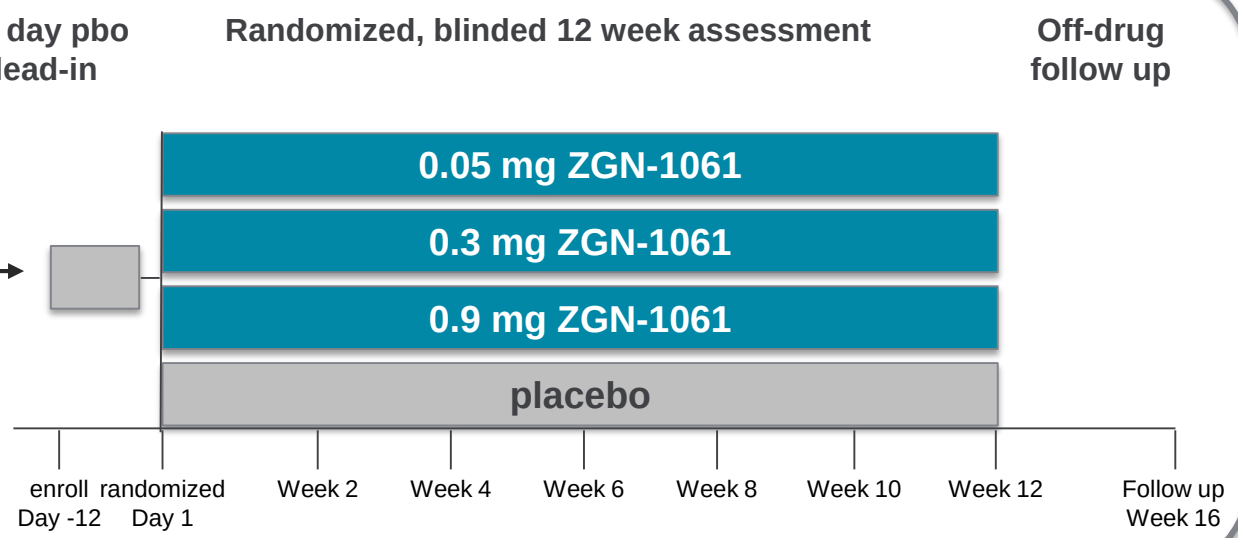
Arrow indicates day that beloranib-treated animals were in extremis (animals euthanized to due to morbidity).

Key Findings

- Pharmacokinetic profile demonstrates rapid exposure and clearance
- Target engagement data supportive of effective exposure
- Efficacy data encouraging and supportive of drug effect
  - Up to approximately one pound/week average weight loss
  - Positive trends across multiple metabolic measures
- Overall safety/tolerability profile is clean, with no impact on sleep
- No prothrombotic effects observed with ZGN-1061
- Results support advancement into Phase 2 clinical trial

ZAF-1061-201: 3 Month Assessment of ZGN-1061 in Individuals with Type 2 Diabetes

- 120 M/F T2DM
- Age 18-65
- BMI ≥ 27
  - A1c 7-11%
  - No insulin
- Low risk for VTE
- Prior bariatric surgery allowed (at least 1 yr post)



- Randomization 3:1 active to placebo
- Study drug administered as SC injection every 3 days (Q3D)

ZAF-1061-201: Study Objectives

To assess the effects of three doses of ZGN-1061 vs. placebo on:

- Primary
  - Glycemic control (HbA1c)
  - Safety and tolerability including coagulation related measures
- Secondary
  - Body weight, waist and hip circumference
  - Supportive measures of glycemic control (fasting glucose, insulin, C-peptide, proinsulin, glucagon)
  - Beta-cell function and insulin sensitivity
  - Preprandial and postprandial glycemic parameters (50 patients)
  - Cardiometabolic, inflammatory, and other biomarkers relevant to obesity and/or T2DM
  - Patient reported outcomes
  - Pharmacokinetics (40 patients)

2Q 2017 Financial Results

Patricia Allen, Chief Financial Officer

2Q 2017 Selected Financial Summary

- Expect to end 2017 with greater than $70 million in cash, cash equivalents and marketable securities
  - Strong position to drive ZGN-1061 forward through planned Phase 2 clinical trial
  - Expect cash balance will extend through calendar year 2018

Balance Sheets	As of June 30, 2017	As of June 30, 2016	As of December 31, 2016
Cash, Cash Equivalents and Marketable Securities	$ 106.0M	$ 150.5M	$ 129.2M
Total Assets	$108.8M	$ 154.8M	$131.6M

Statements of Operations	Quarter Ended June 30, 2017	Quarter Ended June 30, 2016	Quarter Ended December 31, 2016
Research & Development Expenses	$ 10.5M	$ 10.2M	$ 7.3M
General & Administrative Expenses	$ 3.0M	$ 4.9M	$ 3.2M
Net Loss	($ 13.3)M	($ 15.0)M	($ 10.4)M
Net Loss per Share	($0.49)	($0.55)	($0.38)

Conclusion

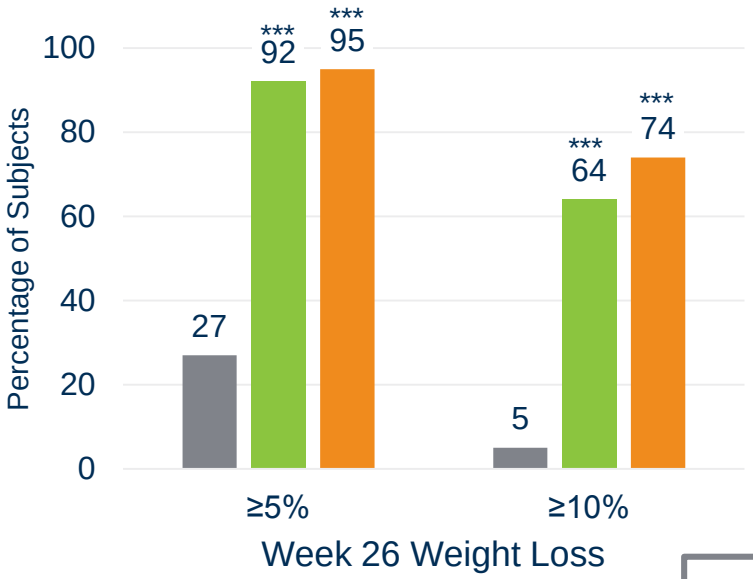
Tom Hughes, Ph.D., President and Chief Executive Officer

MetAP2 Inhibition: Potential for Best-in-Field Impact on Glycemic Control and Weight Loss

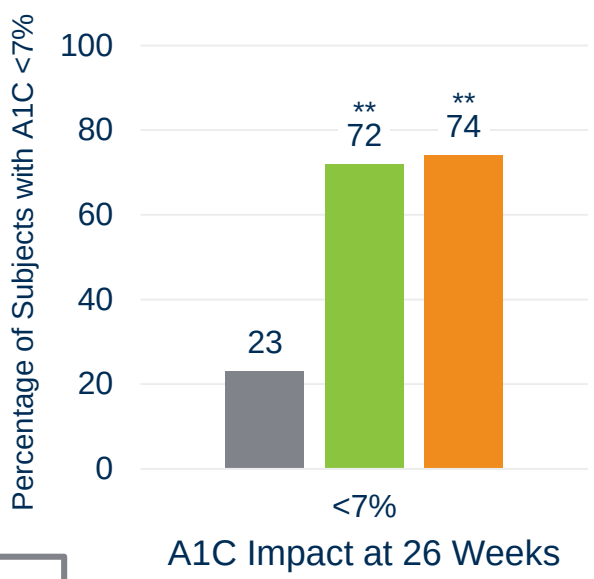
Beloranib Phase 2b ZAF-203 Clinical Trial

>90% of Treated Patients *experienced* **≥5%** weight loss

>60% of Treated Patients *experienced* **≥ 10%** weight loss



Majority of Treated Patients Achieved Key Target A1c Levels of <7%

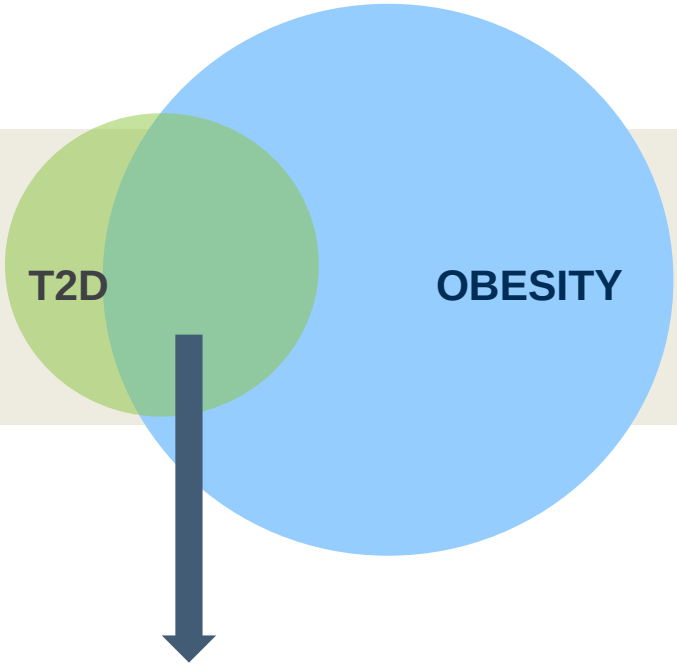


Placebo (N=22)
1.2 mg Beloranib (N=25)
1.8 mg Beloranib (N=19)

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

Unmet Medical Need in Type 2 Diabetes and Obesity

Type 2 Diabetes Market
- 25M patients
- $35B Rx market
- 80% of patients receive Rx
- More treatments needed due to progressive nature of disease



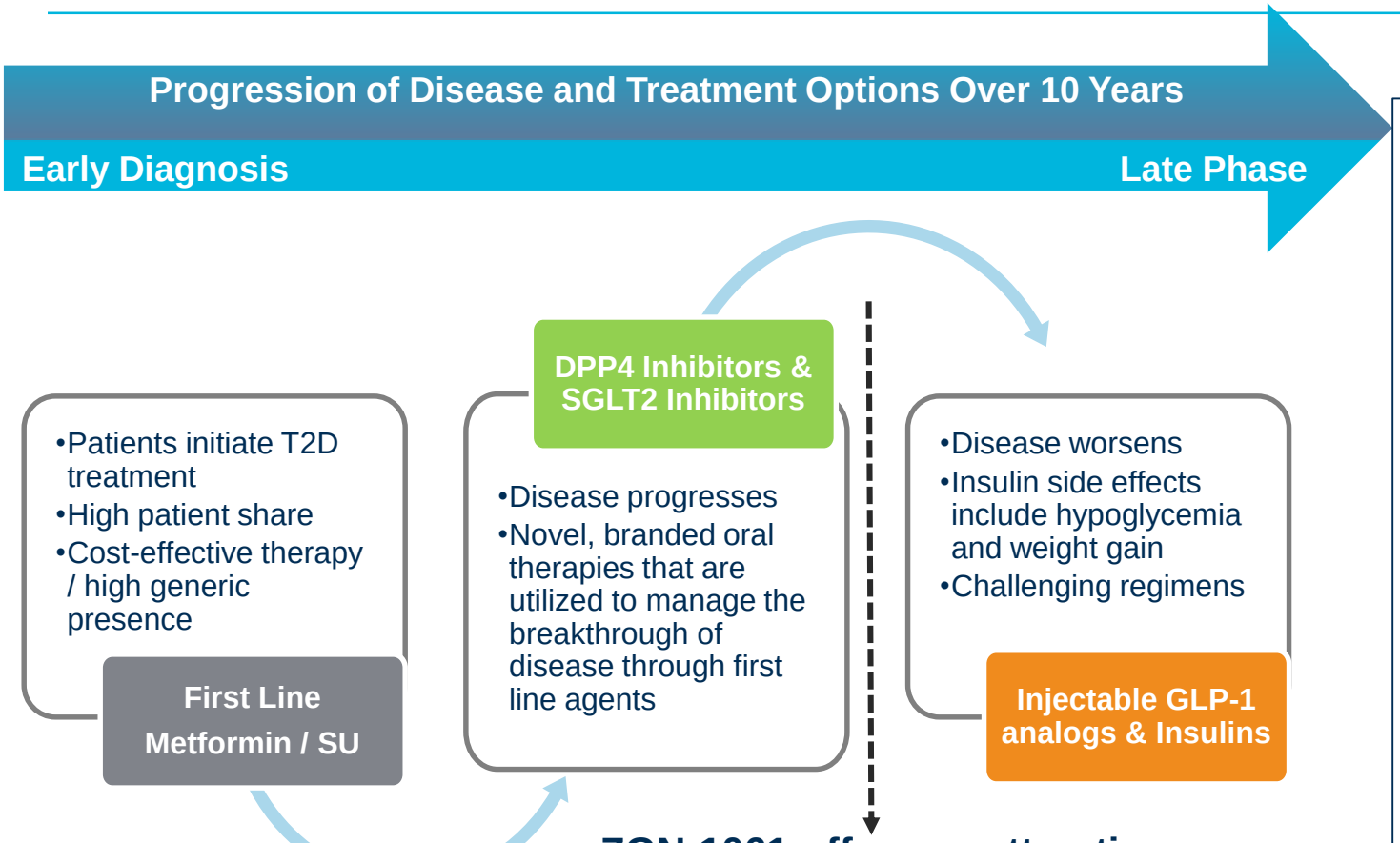
Obesity market
- 100M patients
- $500M Rx market
- 5% of patients receive Rx
- Few treatment options

Opportunity for ZGN-1061 to address patient segments of high unmet need

Patients who have failed numerous Rx options/procedures (bariatric surgery failures, patients who require insulin)

Patient segments defined by poor glycemic control, excess weight, inflammation, hyperlipidemia, and fatty liver

Living with Type 2 Diabetes



ZGN-1061 offers an attractive option for patients with breakthrough disease, approaching or currently on insulin

Patients who progress to injectable therapies may experience:

- Increased body weight (insulin)
- Poor glycemic control
- Hypoglycemia (insulin)
- Nausea (GLP-1)
- Increased CV Risk
- Increased BP
- Co-morbidities and glucose monitoring that increase the costs to manage patients for healthcare systems

2017 R&D Objectives

MetAP2 Portfolio

- ☐ Ongoing research and discovery focused on MetAP2 pathway

ZGN-1061

- ☑ Complete dosing of ZGN-1061 Phase 1 clinical trial by end of Q1; report data in early Q2
- ☑ Report data package on differentiation of ZGN-1061 from beloranib
- ☐ Initiate Phase 2 clinical trial of ZGN-1061 in type 2 diabetes and obesity in Australia and New Zealand in 3Q17
- ☑ Abstracts and presentations regarding ZGN-1061 clinical and nonclinical profile
- ☐ Refine manufacturing to provide Phase 2 and Phase 3 drug supply

Q&A

Thank You