RESULTS: HSG4112 showed desirable changes in phenotype by enhancing ENERGY EXPENDITURE

• HSG4112 treatment showed dose dependent weight reduction for all 3 doses, resulting in average percent weight change at 6 weeks of 12.2%, -3.3% and -26.0% respectively.

• There was dose dependent trend for improvements in insulin sensitivity.

• Leptin and Insulin level were normalized with the administration of HSG4112 for 6 weeks.

• There was dose dependent trend for improvements in insulin sensibility.

• In nonclinical studies, HSG4112, a novel small molecule anti-obesity agent:
  - resulted in dose dependent weight reduction
  - increased O2 consumption
  - increased CO2 generation
  - decreased AMPK activity in hypothalamus which means the increased peripheral energy expenditure
  - normalized leptin level
  - improved insulin sensitivity
  - resulted in mice achieving lean and body shape

• These results suggest HSG4112 as a potential cure for obesity by enhancing energy expenditure and reducing food intake with preventive effect on T2DM.

STUDY DESIGN

• Adiposity efficacy of HSG4112 was tested in DIO mice: HSG4112 was given orally once daily for 7 days for 6 consecutive weeks (q.d.7h/14h).

• The test consisted of total 7 groups: a normal control (normal diet), a vehicle control group (high fat diet), 3 test groups (10mg/kg, 30mg/kg and 100mg/kg) and a positive control group (Sibutramine•HCl 30mg/kg) for 6 weeks.

• Body weight and food intake were measured throughout the study and fat related organ weights as well as the sizes of adipocytes in WAT & BAT were determined at the end of the study to assess the adiposity effect of HSG4112.

• Insulin, leptin, fasting glucose, HbA1c, etc. were additionally measured to evaluate the preventive effect on metabolic syndrome.

• HSG4112 is hydrophobic isoflavonoid NCE with ~350 daltons in molecular weight and > 3.69 of the apparent 1-octanol/water partition coefficient (logD).

• Hypothalamic AMPK activity

• There was dose dependent trend for improvements in insulin sensitivity.

Figure 1. Representative images of mice at the end of the study

Figure 2. Body weight changes

Figure 3. Energy expenditure measurement using CLAMS

Figure 4. Hypothalamic AMPK activity

Figure 5. Leptin (pg/ml) at 6 weeks

Figure 6. Insulin (ng/ml) & Glucose (mg/dL) at 6 weeks

CONCLUSIONS

• Efficacy and Safety of HSG4112, a Novel Small Molecule Anti-Obesity Oral Agent in Diet-Induced Obesity (DIO) Mice

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