**Study Objective**
To evaluate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of single ascending intravenous doses of XOMA 358 in healthy adult male subjects.

**Study Design**
- **Study Design**: Randomized, double-blind, placebo-controlled, single ascending dose (SAD) study.
- **Study Population**: Healthy adult male subjects.
- **Assessment**: Safety outcomes, PK parameters, and pharmacodynamic response.

**Background**
XOMA 358 is a fully human monoclonal antibody to the human insulin receptor (InsR) that allosterically inhibits insulin action both in vitro and in vivo (Kwong et al., 2014). We herein report results from a Phase 1, Double-blind, Placebo-controlled, Single Ascending Dose Study in Healthy Adults.

**Results - PD**
**XOMA 358 Treatment Induced Insulin Resistance**
- Indicated by a dose-related increase in magnitude and duration of AM fasting HOMA-IR.
- Drug-induced severe insulin resistance, as measured by AM fasting HOMA-IR, was evident in all treated groups but was fully evident by Day 2 and persisted for at least 5 days.

**Results - PK**
**XOMA 358 Human Pharmacokinetics Were Better Than Predicted**
- Dose-proportional PK and an elimination half-life longer than expected for a surface receptor-targeted monoclonal antibody.

**Results - Safety**
**XOMA 358 Tolerability**
- No serious AEs; 5 Subjects received Placebo, of which 4 Subjects reported AEs.
- All drug-related AEs were mild (43/46) or moderate (3/46), and none required either concomitant medication or invasive procedures for management.

**Summary & Conclusions**
XOMA 358, a Novel Treatment for Hyperinsulinemic Hypoglycemia: Safety and Clinical Pharmacology from the First in Human Trial

**References**
Benedon S, Mahgerefteh F, Zarate CA, Coggin M, Quinney M, Caro PJ, Begg A, Maggs M. Estrogens and glucose disposal.

**LBS-104**

Hyperinsulinemic hypoglycemia (HI), a complication of non-insulin dependent and Congenital Hyperinsulinism, remains a serious medical concern with limited therapeutic options. We recently described a fully human IgG2 monoclonal antibody XOMA 358 to the human insulin receptor (InsR) that allosterically inhibits insulin action both in vitro and in vivo (Kwong et al., 2014). We herein report results from a Phase 1, Double-blind, Placebo-controlled, Single Ascending Dose Study in Healthy Adults.

**Safety and Pharmacology**
- Dose-related increases in post-prandial glucose levels as evidenced by a 15-minute insulin tolerance test (ITT).
- Circulating insulin levels, considered as a biomarker, are affected at the lowest tested dose (0.1 mg/kg).
- All drug-related adverse events were mild (43/46) or moderate (3/46), and none required either concomitant medication or invasive procedures for management.

**Pharmacokinetics**
- Pharmacokinetics in humans were better than anticipated with a half-life ranging 15-26 days.
- Increases in post-prandial glucose levels were evident by Day 2, and persisted for at least 5 days.

**Pharmacodynamics**
- Drug-induced severe insulin resistance, as measured by AM fasting HOMA-IR, was evident in all treated groups but was fully evident by Day 2 and persisted for at least 5 days.

**XOMA 358 Human Pharmacokinetics Were Better Than Predicted**
- Dose-proportional PK and an elimination half-life longer than expected for a surface receptor-targeted monoclonal antibody.

**Summary & Conclusions**
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