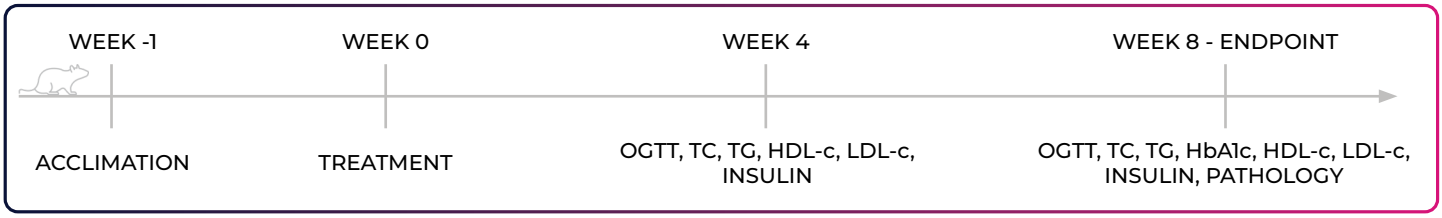
CHEMPARTNER
DEDICATED TO LIFESCIENCE

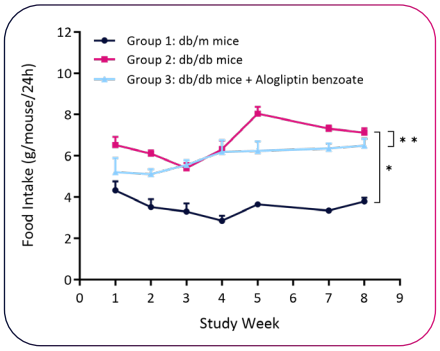
DB/DB AND OB/OB MOUSE MODELS OF TYPE 2 DIABETES AND OBESITY

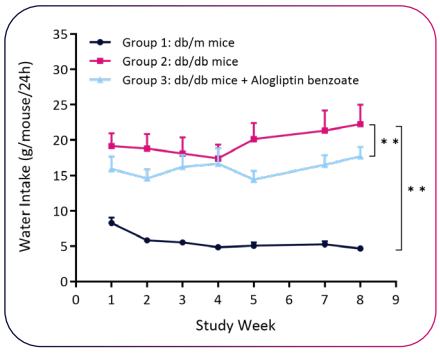
- Obesity has reached epidemic proportions over the past 40 years, leading to huge public health and economic issues due to contribution to several metabolic comorbidities:
  - Insulin resistance
  - Type 2 diabetes (T2D)
  - Liver disease
- Obesity is associated with a chronic, low-grade inflammation, with the gut microbiota emerging as a fundamental environmental factor modulating whole body metabolism
- The liver and adipose tissues play a central role in obesity:
  - Adipose tissue can store and release energy under the form of lipids
  - Adipose tissue is an endocrine organ synthesizing biologically active compounds (i.e., adipokines) that are involved in the regulation of several metabolic pathways
- Leptin is an adipokine that is mainly produced by mature adipocytes and has important roles in the following:
  - Regulation of energy homeostasis
  - Lipid and glucose metabolism
  - Immune response via the cognate leptin receptor
  - Alterations in leptin signaling are closely associated with metabolic disease like obesity and type 2 diabetes
- Type 2 diabetes is a chronic condition linked to persistently high blood sugar levels:
  - Current estimates suggest that ~6% of the world's population have T2D
  - ~$827 billion is spent on diabetes management
  - Main cause is insulin resistance
  - First line management for T2D include lifestyle changes combined with blood sugar monitoring

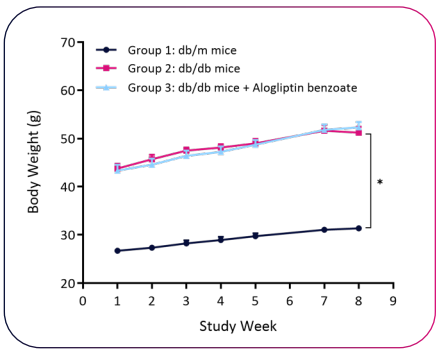
MODEL	DESCRIPTION	ADVANTAGES	LIMITATIONS
db/db mouse	Autosomal recessive point mutation in the leptin receptor gene.	• Most widely used mouse model in T2D (Type 2 Diabetes) research. • Demonstrates obesity, hyperglycemia, glucosuria, hyperphagia, polydipsia, polyuria, and insulin resistance. • Robust – can proceed to severe depletion of pancreatic islets and death by 10 months.	• Different mechanism of wound healing compared to humans. • db/db mice are sterile. • Maintenance requires breeding between db/m pairs.
ob/ob mouse	Homozygous for nonsense mutation in leptin.	• Used in obesity-induced T2D research. • Demonstrates obesity, transient hyperglycemia, glucosuria, hyperphagia, and insulin resistance. • Good model for assessing drugs for use in counteracting hyperphagia associated with obesity and oral hypoglycemic drugs.	• ob/ob females are sterile - can be corrected via leptin treatment. • ob/ob males can occasionally reproduce if maintained on a restrictive diet. • Does not have hypercoagulable blood; therefore, cannot be used for research on cerebrovascular and cardiovascular complications of diabetes.

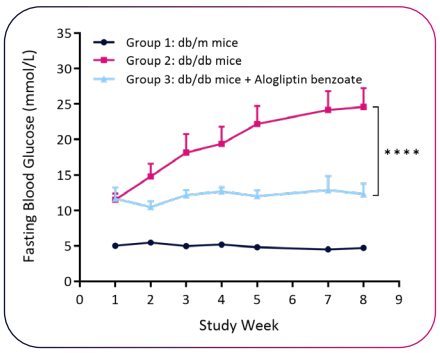
VALIDATED DB/DB PRECLINICAL MOUSE MODEL

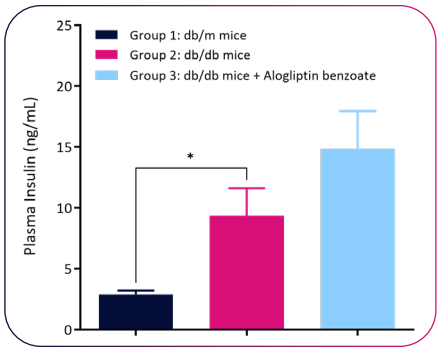


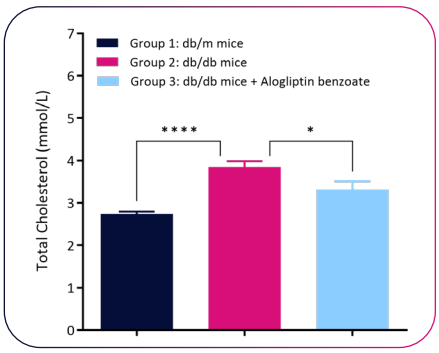


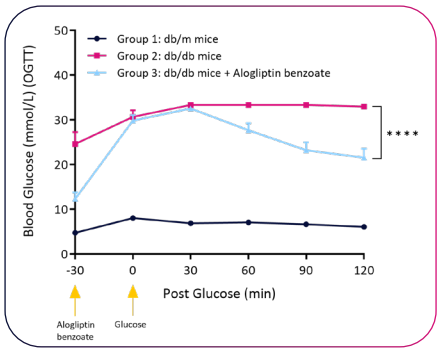


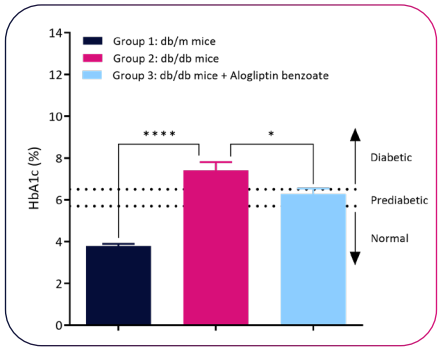


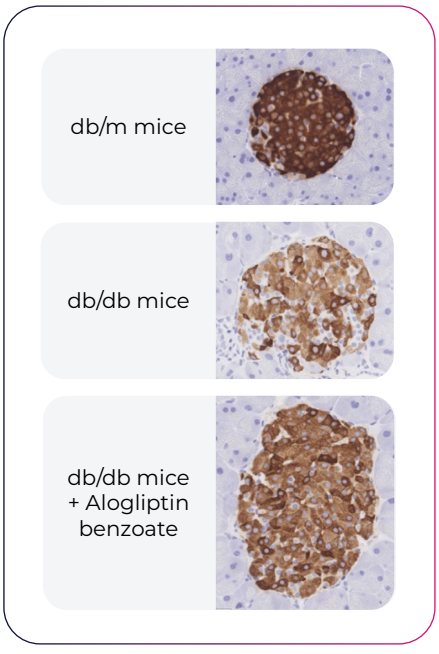








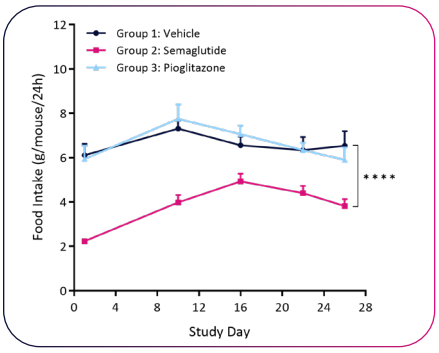


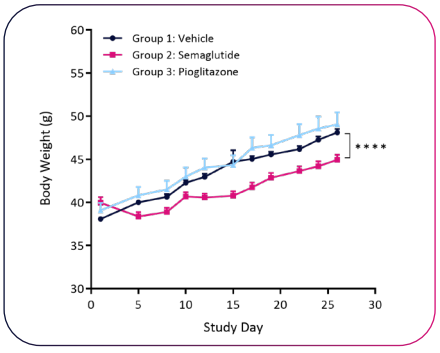


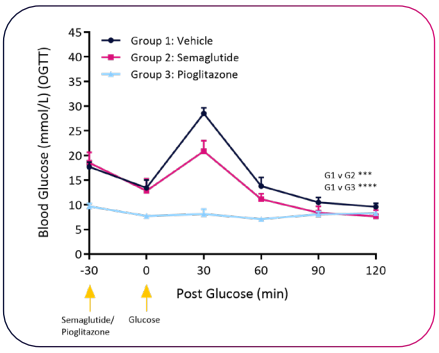
ALOGLIPTIN BENZOATE SoC VALIDATION

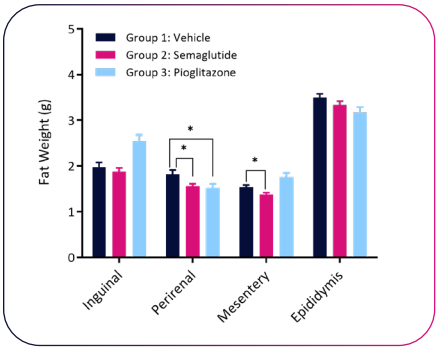
- ✓ No effect on body weight
- ✓ Modest glucose-lowering effect
- ✓ Increased plasma insulin secretion
- ✓ Reduced HbA1c to prediabetic levels
- ✓ Improved glucose tolerance
- ✓ Reduced total cholesterol, triglycerides, HDL-c, LDL-c

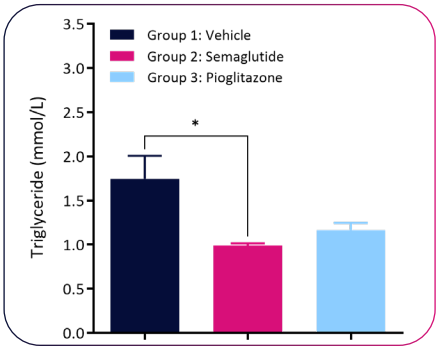
VALIDATED OB/OB PRECLINICAL MOUSE MODEL

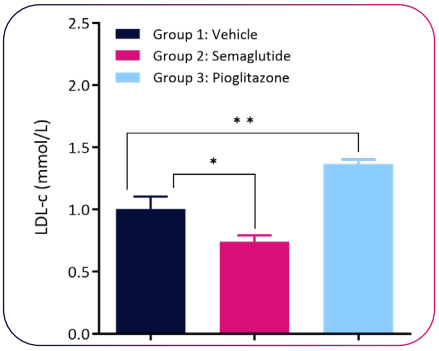












SEMAGLUTIDE SoC VALIDATION

- ✓ Significant reduction in food intake
- ✓ Significant reduction in body weight
- ✓ Modest reduction in blood-glucose concentration
- ✓ Significant reduction in triglycerides and LDL-c
- ✓ Significant reduction in perirenal and mesentery fat weights

PIOGLITAZONE SoC VALIDATION

- ✓ No effect on food intake or body weight
- ✓ Significant reduction in blood-glucose concentration
- ✓ Modest decrease in triglycerides
- ✓ Significant reduction in perirenal fat weight

SUMMARY

The global rising prevalence of type 2 diabetes and obesity warrants the need for robust, well validated preclinical mouse models. With short lead times and a comprehensive range of scientific readouts, our db/db and ob/ob mouse models offer a competitive solution to accelerating your research pipeline.

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