

Established Models

Model	#	Species/strain*	Dose frequency x duration	Sampling frequency	Clinical chem/Assays [#]
DIO	40	mouse, rat/all includes Zucker fatty, DIO-LE	qd x 28day	Weekly x 5	BW, feed intake, QNMR, Leptin, adiponectin
Anti-obesity efficacy: Central model	24	i.c.v. cannulated Rat/all	qd x 14 days	Daily	BW, feed intake, QNMR, leptin, adiponectin
Anti-diabetic efficacy	40	Mouse/rat various: Spontaneous and induced models (i.e., STZ)	qd x 28 days	Weekly x 5	Glucose, insulin, OGTT, BW, ketones, trigs, cholesterol
Euglycemic clamp	18	Rat/all	Acute	5 time-points relative to infusion	GIR, fasted glucose, insulin
In vivo insulin secretion	24	Rat/all	Acute	7 time-points relative to dose	Insulin, glucose, glucagon
OGTT	40	Mouse, rat/all	Acute (compd + glucose bolus)	6 time-points relative to glucose	Glucose, insulin
Fructose/sucrose fed	40	Rat/all	qd x 28 days	Weekly x 5	BW, feed intake, Trigs, chol, Liver trigs
Kagawa	72	ADX SD	Acute (3 injections)	Once	Urine: Na, K
PK study	40	mouse, rat/all	Acute	8 time-points relative to dose	Plasma drug concentration, AUC
Receptor occupancy	120	Rat/SD	Acute	5 time-points relative to dose	Plasma: drug conc Tissue conc. (4 brain regions)
Intestinal transit time	48	Mouse/rat	Acute	5 time-points	% of small intestine length
Telemetry BP	36	Rat/all Spontaneous and induced hypertension	qd x 14 days	Continuous monitoring	Diastolic/systolic and mean BP with HR
Renal models	36	Mouse, rat: various Spontaneous and induced models	qd x 42 days	Weekly x 8	Plasma: BUN, Cr, MCP-1 Urine: volume, protein, Cr Histology, renal weight
Ethanol induced gastric ulcer	24	Rat/all	Acute	Terminal	Stomach # and grading of lesion
Early Tox Assessment	40	Rat/all	qd x 14 days	Terminal	Renal ,Cardiac ,endocrine and Inflammatory panel: histology

- *all strains are available
- [#] Many other analytes available than those indicated for these representative studies

Renal models: STZ—rat, ZDF, ZSF1, ZDSD, aldo infusion (nephrectomized, salt loaded aldo infused rat), angiotensin II infused db/db mouse, Tacrolimus induced, cyclosporine induced, renal mass reduction