

Melior Discovery, Inc.

Word-Class Preclinical In Vivo Pharmacology

Pioneer in Drug Repositioning and In Vivo Phenotypic Screening

*thera*TRACE[®]-Suited Models & Comprehensive LIST OF ALL MODELS

SEPTEMBER 2021



theraTRACE® Platform-Suited Assays



Click on assay name to go to web page

Acetylcholine Writhing Allergic Contact Hypersensitivity **Bleed Time Blood Analysis Clinical Chemistries Collagen Induced Arthritis Colonic Propulsion Delayed-Type Hypersensitivity** DFXA **Diet-Induced Obesity DSS-Induced Colitis** Experimental Autoimmune Encephalomyelitis Fecal Output Food Intake Forced Swim Test Formalin Analgesia Assay Gastrointestinal Transit Grip Strength Hot Plate Assay Insulin Tolerance Test (ITT) Irwin Light Dark Transitions

LPS- Pulmonary Inflammation LPS- Systemic Inflammation Maximal Electroshock Metabolic Hormone Levels Micturition – Diuretic-Induced Stress Monocyte Infiltration Morphine-Induced Constipation MPTP-Induced Parkinson's Disease Open-Field Activity Oral Glucose Tolerance Test (OGTT) Pentylenetetrazol-Induced Seizures Pulmonary Allergic Asthma Rotarod Sebum Production Stress-Induced Fecal Production Stress-Induced Hyperthermia Stress-Induced Corticosterone Tail Suspension **Tail-Flick** von Frey/Carrageenan Sensitivity Weight Gain





LIST OF VALIDATED MODELS





Cardiovascular:

Assay	Validating Compound	Parameters	Species	Comments
Ploading Time *	Heparin	Time to bleeding cessation	Mouse,	Short lead time required,
Bleeding Time *			Rat	Good reproducibility
Blood Pressure Tail Cuff	Nifedipine	Blood pressure and heart rate	Rat	Short lead time required,
				Group size n>12
	Candesartan	SHR Rats	Mouse,	Surgically complex
Hypertension/Telemetry		Blood Pressure/MAP	Rat	
		Heart Rate		

Gastrointestinal:

Assay	Validating Compound	Parameters	Species	Comments
Colonia Propulsion *	Morphine	Latency to colonic expulsion of glass	Mouse,	Short lead time required,
<u>Colonic Propulsion ·</u>		bead	Rat	Good reproducibility
DSS Model of Colitie *	Cyclosporin A	Body Weight	Mouse	Short lead time required,
DSS – Wodel of Collus ·		Gastrointestinal distress		Good reproducibility
Focal Output *	Morphine	Fecal pellet count	Mouse,	Short lead time required,
			Rat	Good reproducibility
Gestrointesting Transit *	Morphine	Intestinal distance traveled of gavage –	Mouse,	Short lead time required,
<u>Gastronitestinar Transit</u>		administered charcoal bolus	Rat	Good reproducibility
IBS and Acetylcholine Writhing *	Morphine	Time to writhing onset	Mouse,	Short lead time required,
		Number of writhes	Rat	Good reproducibility
Morphine Induced Constinution *	Naloxone	Latency of colonic expulsion of glass	Mouse,	Short lead time required,
		bead	Rat	Good reproducibility

Hair Growth and Dermatitis:

Assay	Validating Compound	Parameters	Species	Comments
Allergic Contact Hypersensitivity *	Dexamethasone	Swelling of ears sensitized to oxazolone, PPD, or DNFB Clinical evaluation of ear redness, Cytokine/IL levels in ear biopsies, INF - γ	Mouse, Rat	Short lead time required, Good reproducibility
<u>Delayed – Type Hypersensitivity</u>	Dexamethasone	Footpad thickness after immunogenic challenge	Mouse, Rat	Short lead time required, Good reproducibility
Hair Growth Assay	Minoxidil	Hair growth score, Time and magnitude	Mouse	Chronic Model
Sebum Production *	Isotretinoin	Sebum production, Fur water retention	Mouse	Ideally treatment is continued for 2-3 weeks
Pruritis Scratching	U-50,488	Total scratching events over 30-minute period	Mouse	Variable duration depending on pruritis- inducing agent





Infectious Disease Validating Compound **Parameters** Species Comments Can be adjusted, by inoculation titer to Oseltamivir (Tamiflu®) Survival, Body weight, SpO2 Mice Influenza lethal vs. sublethal Acute model, TNF-(and IL-6 blood levels after Mouse, Rat Short lead time required, **Sepsis** Dexamethasone lipopolysaccharide challenge Good reproducibility

Inflammation and Arthritis:

Assay	Validating Compound	Parameters	Species	Comments
Acute Nephritis	DL-propargylglycine (PAG)	Blood (BUN, CRE, Sodium) and urine (CRE, Protein) chemistries	Rat	Short lead time required
Acute Pancreatitis	DL-propargylglycine (PAG)	Markers of pancreatic injury (Serum Amylase, Pancreatic Myeloperoxidase)	Mouse	Short lead time required
	Dexamethasone	Swelling of ears sensitized to oxazolone,	Mouse,	Short lead time required,
		PPD, or DNFB	Rat	Good reproducibility
Allergic Contact Hypersensitivity *		Clinical evaluation of ear redness,		
		Cytokine/IL levels in ear biopsies, INF -		
	Morphine	Pain responsiveness after Cansaicin	Rat	Short lead time required
Capsaicin Hyperalgesia Assay	Worphine	inflammation	Kut	Good reproducibility
	Dexamethasone	Clinical evaluation of paw and joint	Mouse,	Strain sensitive,
Collagen Induced Arthritis*		inflammation	Rat	Short lead time required,
				Good reproducibility
Deleved Type Hypersonsitivity*	Dexamethasone	Footpad thickness after immunogenic	Mouse,	Short lead time required,
Delayed Type Hypersensitivity		challenge	Rat	Good reproducibility
EAE Model of Multiple Sclerosis *	FTY 720	Clinical Scores	Mouse,	Strain and supplier sensitive
EAE Model of Multiple Scierosis		Body weight	Rat	Good reproducibility
Formalin Analgesia Assay*	Oxycodone	Duration of Phase I (acute) pain,	Mouse,	Short lead time required,
<u>Pointaini Anargesta Assay</u>		Duration of Phase II (delayed) pain	Rat	Good reproducibility
	Dexamethasone	Cytokine and MCP-1 levels in dissected	Mouse,	Acute model,
<u>LPS – Pulmonary Inflammation *</u>		lung tissue,	Rat	Short lead time required,
		Cellular infiltrate analysis		Good reproducibility
	Dexamethasone	TNF-(and IL-6 blood levels after	Mouse,	Acute model,
<u>LPS – Systemic Inflammation*</u>		lipopolysaccharide challenge	Rat	Short lead time required,
				Good reproducibility
Monocyte Infiltration *	Dexamethasone	MCP-1 levels from peritoneal lavage,	Mouse,	Short lead time required,
		Differentials	Rat	Good reproducibility
	Dexamethasone	Cytokine and MCP-1 levels in dissected	Mouse,	Ovalbumin: Chronic Model,
Pulmonary Allergic Asthma*		lung tissue,	Rat	Short lead time required,
		Cellular infiltrate analysis		Good reproducibility
Zymosan-A Induced Peritonitis	Dexamethasone	Zymosan-A induces leukocyte	Mouse	Short lead time required,
Zymosan-A induced Peritonitis		accumulation in the peritoneum		Good reproducibility





Metabolic:

Assay	Validating Compound	Parameters	Species	Comments
db/db Mouse Model	Rosiglitazone	Multiple parameters: Chronic glucose, Hormones, HbA1c, pancreatic insulin, IHC	Mouse	Chronic, Good reproducibility
DEXA *	N/A	Bone parameters and body composition (fat and lean) parameters	Mouse	Coupled with high fat diet, Good reproducibility
Diet Induced Obesity	Rimonabant	Body composition (fat and lean), Weight change over time, Glycemic control parameters (FPG, OGTT, ITT)	Mouse, Rat	Good reproducibility
Diet Induced Obesity/High- Fat Diet *	Rimonabant	Quantity of food ingested per day and per gram of body weight, Weight change over time, Weight change from initial measurement, DEXA analysis, Serum markers for Leptin, Insulin, and Adiponectin	Mouse, Rat	Can be coupled with multiple assays, Short lead time required, Good reproducibility
Euglycemic/Hyperglycemic Clamp Study	N/A	Hyperinsulinemic euglycemic clamp, Glucose infusion rate to maintain euglycemia with constant insulin infusion rate	Mouse, Rate	Gold standard measure of insulin sensitivity
Food Intake *	Imipramine	Quantity of food ingested per day and per gram of body weight, Food ingested after fasting	Mouse, Rat	Short lead time required, Good reproducibility
Insulin Tolerance Test (ITT)*	Insulin	Glucose response to insulin	Mouse, Rat	Can be coupled with multiple assays Short lead time required, Good reproducibility
mHFD-Induced NASH Model	Obeticholic Acid	Multiple parameters: Weight change from initial measurement, Glycemic control parameters (OGTT, ITT), Fasting ALT and Serum Triglycerides	Mouse	Good reproducibility
<u>mHFD-Induced NASH</u> Model/Enhanced Fibrosis	Obeticholic Acid	Multiple parameters: Weight change from initial measurement, Glycemic control parameters (OGTT, ITT), Serum Triglycerides/Cholesterol, ALT/AST levels, Hydroxyproline levels	Mouse	Variation of mHFD-Induced NASH model utilizing CCL4 Good reproducibility





Assay	Validating Compound	Parameters	Species	Comments
	Rimonabant	Leptin, insulin, adiponectin, c-peptide,	Mouse,	Coupled with multiple metabolic assays,
Matabalia Hormona Lavala *		etc. in response to multiple challenges	Rat	Short lead time required,
Wetabolic Hormone Levels		(high fat diet, drug treatment,		Good reproducibility
		acute/chronic)		
	Rosiglitazone	Multiple parameters: chronic glucose,	Mouse	Chronic,
ob/ob Mouse Model		hormones, HbA1c, pancreatic insulin,		Good reproducibility
		IHC		
Oral Clusosa Talaranaa Tast	Metformin	Glucose levels over a trial period after	Mouse,	Can be coupled with high fat diet model,
(OCTT) *		glucose challenge,	Rat	Short lead time required,
(0011) ·		Pre/Post- High fat diet regimen		Good reproducibility
	Insulin	Multiple parameters,	Mouse,	Metabolic Type I Diabetes,
Strantozotogin Indugad Diabatas		Chronic glucose, hormones,	Rat	Highly specialized,
Streptozotochi-induced Diabetes		HbA1c,		Well - characterized
		Diuresis and Nephropathy		
Weight Gain *	Imipramine	Weight change from initial measurement,	Mouse,	Short lead time required,
		Weight change per day	Rat	Good reproducibility
	Insulin	Multiple parameters,	Rat	Short lead time required,
ZDF Rats		Chronic glucose, hormones, HbA1c,		Good reproducibility
		pancreatic insulin, IHC		





Assay	Validating Compound	Parameters	Species	Comments
Electromyography (EMG)	N/A	Flexor (C-fiber), la, H reflex aptitudes	Rat	Highly specialized capability
		Force exerted to hold onto a wire screen	Mouse,	ALS model
Grip Strength *	N/A		Rat	Fast turn-around time,
				Can be coupled with other assays
Hermeline Induced Tremor	Propranalal	Body tremor (tremor ratio)	Mouse,	Fast turn-around time,
<u>Harmanne-muuceu Hemor</u>	Fiopianoloi		Rat	Good reproducibility
Locomotor and Open Field		Locomotor parameters in an automated	Mouse,	Typically coupled with other assays,
Activity *	Risperidone	open-field	Rat	Short lead time required,
Activity				Good reproducibility
		Tibialis anterior and plantaris response	Mouse	ALS model
Motor Evoked Potentials	N/Δ	latencies,		Strain and supplier sensitive,
(CMAP)	IV/A	Behavioral evaluation (limp splay, toe		Good reproducibility
		spread)		
		Time to T-turn	Mouse	Fast turn-around time,
Pole Test *	N/A			Can be repeated over time,
				Good reproducibility
Poterod *	Haloparidal	Coordination,	Mouse,	Primarily utilized as pharmacology safety
Kotarou	Haloperidol	Acceleration	Rat	assay

Neurology:

Assay	Validating Compound	Parameters	Species	Comments
	Valproate	Seizure exhibition	Mouse	Epilepsy
6-Hz Psychomotor Seizure				Fast turn-around time,
				Good reproducibility
	Amantadine	Rotational behavior,	Rat	Newly developed,
6-OHDA Lesion		Dopaminergic markers,		Neurodegenerative symptomatic
		Dyskinesias		Parkinson's disease model
Audiogania Saigura/EMD1	R-baclofen	Locomotor activity,	Mouse	Fragile X Model
Knockout		Seizure (score 0-4)		Short lead time required,
KIIOCKOUL				Good reproducibility
Catalanan *	Haloperidol	Reversal of haloperidol-induced	Mouse	Newly developed
Catalepsy		cataleptic response		
Experimental Autoimmune	FTY 720	Clinical scores,	Mouse,	Strain and supplier sensitive,
Encephalomyelitis (EAE)		Body weight	Rat	Good reproducibility
EEG Pro- and Anti- Convulsant	Diazepam,	Sub-clinical seizure threshold in response	Mouse,	Highly specialized capability
<u>Evaluation</u>	Pentylenetetrazol	to seizure-inducing agents	Rat	
		Axial, limb and orolingual AIMs	Rat	Neurodegenerative model of Parkinson's
L DOPA Induced Dyskinesis	Amontodino			Disease,
L-DOPA mouceu Dyskinesia	Amantadine			Short lead time required,
				Good reproducibility





Lithium Pilocarpine Status	Diazepam,	Cortical EEG activity in response to	Rat	CNS/Epilepsy,
Epilepticus	Pilocarpine	pilocarpine-induced SE		Short lead time required,
				Good reproducibility
Maximal Electroshock *	Phenytoin	Seizure (presence/absence)	Mouse	6 Hz seizure,
				Short lead time required,
				Good reproducibility
MPTP-induced Parkinson's	L-deprenyl	Locomotor parameters in an automated	Mouse	Neurodegenerative model of Parkinson's
Disease *		open-field apparatus,		Disease,
		Striatal dopamine levels,		Strain and supplier sensitive,
		Dopamine cell number (TH staining;		Short lead time required,
		substantia nigra)		Good reproducibility
Pentylenetetrazol-Induced	Diazepam	Time to initial colonic seizure,	Mouse,	CNS/Epilepsy,
<u>Seizures *</u>		Time to initial tonic seizure,	Rat	Short lead time required,
		EEG measurements		Good reproducibility
Rett Syndrome	N/A	Locomotor,	Mouse	Neurodegeneration/Rett Syndrome,
Neurodevelopment Model		Respiration,		Breeding limitations,
		Seizure,		Actively breeding colony
		Mortality		
Startle Prepulse Inhibition *	Risperidone	Sensorimotor gating	Mouse	Short lead time required,
				Good reproducibility,
				Group sizes n>10

Neurophysiology:

Assay	Validating Compound	Parameters	Species	Comments
C-fiber Pain Reflex	N/A	Flexor (C-fiber), la, H reflex aptitudes	Rat	Muscle response, spasticity
Electromyography (EMG)		-		Highly specialized capability
Cortical EEG Frequency	N/A	Cortical EEG activity evaluated as	Mouse,	Highly specialized capability
		function of frequency	Rat	
Cortical Sensory Evoked	N/A	Cortical response to peripheral sensory	Rat	Cognitive disorders (Schizophrenia, Stroke,
Potentials		stimulus		Head Injury),
				Highly specialized capability
EEG Sleep/Wake and Motor	Caffeine, Modafinil,	Sleep architecture,	Mouse,	Highly specialized capability
Activity	Pentobarbital	Circadian rhythm,	Rat	
		Sleep/wake enhancement,		
		CNS drug side-effects		
Motor Evoked Potentials and	N/A	Nerve conduction velocity,	Rat	ALS, Motor Neuron Diseases,
Nerve Conduction		Neuromuscular function		Highly specialized capability
Proprioceptive Spinal Reflexes	N/A	H/M response amplitude	Rat	Highly specialized capability
Pro- and Anti-Convulsant	Diazepam,	Sub-clinical seizure threshold in response	Mouse,	Highly specialized capability
Evaluation	Pentylenetetrazol	to seizure-inducing agents	Rat	
Subthalamic Nucleus (STN)	N/A	STN bursting patterns	Rat	Neurodegenerative model of Parkinson's
Recording in vivo				Disease,
				Highly specialized capability





Validating Compound Assay **Parameters Species** Comments Breast: EMT6 Conducted in immune competent animals Cyclophosphamide Tumor growth kinetics Mouse Lung: LL/2 (LLC1) Cyclophosphamide Tumor growth kinetics Mouse Conducted in immune competent animals Fibrosarcoma: WEHI164 Tumor growth kinetics Mouse Conducted in immune competent animals Melanoma: B16-F10 Tumor growth kinetics Conducted in immune competent animals Mouse Pancreatic: Pan01 Tumor growth kinetics Mouse Conducted in immune competent animals

Pain:

Assay	Validating Compound	Parameters	Species	Comments
Acetylcholine Writhing *	Morphine	Time to onset of writhing,	Mouse	Short lead time required,
		Number of writhes		Good reproducibility
Capsaicin Hyperalgesia Assay	Morphine	Pain responsiveness after capsaicin	Rat	Short lead time,
		inflammation		Good reproducibility
Chemotherapy-Induced	Morphine	Pain response after chemotherapy	Rat	In development
<u>Neuropathy</u>				
Chronic Constrictive Injury	Gabapentin	Pain responsiveness after sciatic	Mouse,	Surgically complex and specialized,
		constriction	Rat	Chronic model,
				Group sizes of n=10
Cold Response	Morphine	Latency to paw withdrawal from cold	Mouse,	Short lead time required,
		water bath	Rat	Group sizes n>10
<u>Diabetic Neuropathy –</u>	Streptozotocin	Development of neuropathies in STZ-	Rat	Chronic study,
Streptozotocin Rat Model		treated rats		Specialized study
Formalin Analgesia Assay *	Oxycodone	Duration of Phase I (acute) pain,	Mouse,	Short lead time,
		Duration of Phase II (delayed) pain	Rat	Good reproducibility
Hargreaves Hyperalgesia *	Morphine	Radiant heat response	Mouse,	Short lead time,
			Rat	Good reproducibility,
				Group size n>10
Hot Plate *	Morphine	Latency to pain response	Mouse,	Short lead time,
			Rat	Good reproducibility
Migraine	Sumatriptan	Periorbital pain response after	Rat	Newly developed,
		prostaglandin brain infusion		Highly specialized
Spinal Nerve Ligation	Gabapentin,	Paw withdrawal threshold in response to	Rat	Model of neuropathic pain,
	Morphine	von Frey filaments		Good reproducibility
Tail-Flick *	Morphine	Tail heat response,	Rat	Short lead time,
		Lamp or tail immersion		Good reproducibility
Tail Immersion	Morphine,	Measures spinally-driven aspects of pain,	Mouse	Short lead time,
	Oxycodone	Tail heated water bath response		Good reproducibility
von Frey/Carrageenan	Indomethacin	Pain responsiveness after carrageenan	Mouse,	Short lead time,
Sensitivity *		inflammation	Rat	Good reproducibility





Psychiatric and Cognitive:

Chronic Mild Stress	Assay	Validating Compound	Parameters	Species	Comments
Controserone Levels* and/or immunological stress, Coupled stress-induced feed coluptit Gend reproducibility, Group sizes n>12 Chronic Mild Stress- Erad Diazepam Core body temperature in response to stress Mouse, Rat Short lead time, Good reproducibility Chronic Mild Stress- Tail Desipramine Response in depression assay after detronic stress Mouse, Rat Short lead time, required, Good reproducibility, Rat Elevated Plus Marze Diazepam Time in open vs. closed arms Mouse, Rat Short lead time required, Good reproducibility, Group sizes no10 Fear Conditioning Rolipram Contextual memory Mouse Newly developed, Group sizes no10 Forced Swim Test * Imigramine Diazepam Ratio in time in light and dark spaces Mouse Short lead time required, Good reproducibility, Group sizes no10 Kored Object Recognition Test Scopolamine Visual spatial navigation Mouse, Recognition index Short lead time required, Good reproducibility Novel Object Recognition Test Scopolamine Cognition, Recognition index Rat Good reproducibility Open-field Activity * Risperidone Cognition, Recognition index Rat Good reproducibility Socio	Chronic Mild Stress –	Desipramine	Corticosterone levels after physical	Mouse,	Chronic study,
Convel Mid Stress - Stresse Diazepam Core body temperature in response to stress Mouse, Rat Good reproducibility Induced IVperthermia * Desipramine Response in depression assay after chronic stress Mouse, Rat Good reproducibility Chonic Mid Stress - Tail Desipramine Response in depression assay after chronic stress Mouse, Rat Good reproducibility Elevated Plus Maze Diazepam Time in open vs. closed arms Mouse, Mouse, Stress = 0:10 Stort lead time required, Group sizes = 0:10 Fear Conditioning Rolipram Contextual memory Mouse, Group sizes = 0:10 Stort lead time required, Group sizes = 0:10 Forced Swim Test * Imipramine Duration of behavioral despair Mouse, Group sizes = 0:10 Morris Water Maze Scopolamine Visual spatial navigation Mouse, Group sizes = 0:10 Morris Water Maze Scopolamine Cognition, Recognition index Mouse, Group sizes = 0:10 Novel Object Recognition Test Scopolamine Coordination, Recognition index Mouse, Reat Immerespondentibility Open-field Activity * Risperidone Coordination, Acceleration Mouse, Reat Short lead time required, Grood reproduc	Corticosterone Levels *	-	and/or immunological stress,	Rat	Good reproducibility,
Chronic Mild Stress-Stresse Diazepam Core body temperature in response to stress Mouse, Rat Short lead time, Good reproducibility Chronic Mild Stress - Tail Desigramine Response in depression assay after chronic stress Mouse, Rat Chronic study, Good reproducibility Elevated Plus Maze Diazepum Time in open vs. closed arms Mouse, Rat Short lead time required, Goog sizes n>10 Fear Conditioning Rolipram Contextual memory Mouse Newly developed, Group sizes n>10 Forced Swim Test * Diazepum Ratio in time in light and dark spaces Mouse, Group size n>10 Short lead time required, Group size n>10 Morris Water Maze Scoopolamine Visual spatial navigation Mouse, Rat Short lead time required, Group sizes n>10 Morris Water Maze Scoopolamine Visual spatial navigation Mouse, Rat Short lead time required, Good reproducibility Open-field Activity * Risperidone Coordination, Recognition index Rat Good reproducibility Open-field Activity * Risperidone Coordination, Rat Mouse, Short lead time required, Good reproducibility Social Recognition Armodafinil Short term menory, Rat<			Coupled stress-induced fecal output		Group sizes n>12
Induced Hyperhemia* stress Rat Good reproducibility Chronic Midd Stress - Tail Designamine Response in depression assay after chronic stress Mouse, Rat Coord reproducibility, Good reproducibility, Rat Good reproducibility, Good reproducibility, Caroup sizes n-10 Elevated Plus Maze Diazepam Time in open vs. closed arms Mouse, Rat Good reproducibility, Group sizes n-10 Fear Conditioning Rolipram Contextual memory Mouse Newly developed, Group sizes n-10 Forced Swim Test # Imipramine Duration of behavioral despair Mouse Short lead time required, Good reproducibility, Group sizes n-28 Light Dark Transitions * Diazepam Ratio in time in light and dark spaces Mouse Newly developed, Group sizes n-10 Morris Water Maze Scopolamine Visual spatial navigation Mouse, Rat Good reproducibility Novel Object Recognition Test Scopolamine Cognition index Rat Good reproducibility Recognition Rat Good reproducibility Coord net assay, Group sizes n-10 Mouse, Rat Typically coupled with other assay, Group sizes n-10 Mouse Primarily uil/zed as pharmacology safety	Chronic Mild Stress - Stress-	Diazepam	Core body temperature in response to	Mouse,	Short lead time,
Chronic Mild Stress – Tail Designation Response in depression assay after chronic stress Mouse, Rat Chronic study, Good reproducibility Elevated Plus Maze Diazepam Time in open vs. closed arms Mouse, Rat Short lead time required, Good reproducibility, Group sizes n-10 Fear Conditioning Rolipram Contextual memory Mouse Newly developed, Group sizes n-10 Forced Swim Test * Imipramine Duration of behavioral despair Mouse Short lead time required, Group sizes n-10 Light Dark Transitions * Diazepam Ratio in time in light and dark spaces Mouse Newly developed, Group sizes n-10 Morris Water Maze Scopolamine Visual spatial navigation Mouse,	Induced Hyperthermia *	*	stress	Rat	Good reproducibility
Suspension Test chronic stress Rat Good reproducibility Elevated Plus Maze Diazepam Time in open vs. closed arms Mouse, Short lead time required, Good reproducibility, Group sizes n>10 Fear Conditioning Rolipram Contextual memory Mouse Nowly developed, Group sizes n>10 Forced Swim Test Imipramine Duration of behavioral despair Mouse Short lead time required, Good reproducibility, Group size n>8 Light Dark Transitions * Diazepam Ratio in time in light and dark spaces Mouse Newly developed, Group size n>10 Morris Water Maze Scopolamine Visual spatial navigation Rat Good reproducibility Nevel Object Recognition Test Scopolamine Cognition, Recognition index Rat Good reproducibility Open-field Activity * Risperidone Locomotor parameters in an automated open-field Activity * Mouse, Rat Typically coupled with oher assay, Acceleration, Acceleration Fat Short lead time required, Good reproducibility Social Recognition Armodafinil Short term memory, Acceleration Rat Short lead time required, Good reproducibility Startice Prepulse Inhibition * Risp	Chronic Mild Stress – Tail	Desipramine	Response in depression assay after	Mouse,	Chronic study,
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Elevated Plus Maze Rat Good reproducibility, Group sizes n>10 Fear Conditioning Rolipram Contextual memory Mouse Newly developed, Group sizes n>10 Forced Swim Test * Imipramine Duration of behavioral despair Mouse Short lead time required, Good reproducibility, Group sizes n>10 Light Dark Transitions * Diazepam Ratio in time in light and dark spaces Mouse, Mouse, Stort lead time required, Group sizes n>10 Morris Water Maze Scopolamine Visual spatial navigation Mouse, Rat Short lead time required, Group sizes n>10 Novel Object Recognition Test Scopolamine Cognition, Rat Mouse, Rat Inter-experiment variability Open-field Activity * Risperidone Locomotor parameters in an automated one-field Mouse, Rat Typically coupled with other assays, open-field Social Recognition Armodafinil Short tead time required, Good reproducibility Good reproducibility Social Recognition Armodafinil Short tead time required, Good reproducibility Good reproducibility Startle Prepulse Inhibition * N/A Fecal counts after restraint stress, Coupled with corticosterone levels Rat Good reproducibility Startle Prepulse Inhibition * N/A Fecal counts after restraint stress, Coroup sizes n>10 Mouse, Group sizes n>10 Stress-Induced Fecal Producti		Diazepam	Time in open vs. closed arms	Mouse,	Short lead time required,
Group sizes n>10 Fear Conditioning Rolipram Contextual memory Mouse Newly developed, Group sizes n>10 Forced Swim Test * Imipramine Duration of behavioral despair Mouse Short lead time required, Good reproducibility, Group size n>8 Light Dark Transitions * Diazepam Ratio in time in light and dark spaces Mouse Short lead time required, Good reproducibility, Group sizes n>10 Morris Water Maze Scopolamine Visual spatial navigation Mouse, Rat. Good reproducibility Novel Object Recognition Test Scopolamine Cognition, Recognition index Rat Open-field Activity * Open-field Activity * Risperidon Locomotor parameters in an automated open-field Activity * Mouse, Primarily utilized as pharmacology safety Acceleration Social Recognition Armodafinil Short tead time required, Good reproducibility Social Recognition * Risperidone Sensorimotor gaing Mouse, Mouse, Open-field Activity * Social Recognition Armodafinil Short tead time required, Good reproducibility Good reproducibility Social Recognition * Rat assay Short tead time required, Good reproducibility, Group si	Elevated Plus Maze	× ×		Rat	Good reproducibility,
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Group sizes n>10	Vogel Water Conflict	Diazepam	Avoidance behavior to shock	Rat	Newly developed,
					Group sizes n>10





Pulmonary:

Assay	Validating Compound	Parameters	Species	Comments
<u>LPS – Pulmonary Inflammation *</u>	Dexamethasone	Cytokine and MCP-1 levels in dissected	Mouse,	Acute model,
		lung tissue,	Rat	Short lead time required,
		Cellular infiltrate analysis		Good reproducibility
Pulmonary Allergic Asthma*	Dexamethasone	Cytokine and MCP-1 levels in dissected	Mouse,	Ovalbumin
		lung tissue,	Rat	Chronic Model,
		Cellular infiltrate analysis		Short lead time required,
				Good reproducibility
Respiratory Depression	Morphine	Pulse Oximetry (O2 saturation)	Mouse,	Short lead time required,
			Rat	Good reproducibility

Tissue Repair:

Assay	Validating Compound	Parameters	Species	Comments
Liver Fibrosis	N/A	Hydroxyproline, AST, and ALT levels	Mouse	Short lead time required,
		after CCL4 treatment		No positive control available
Pulmonary Fibrosis	Nintedanib	Hydroxyproline levels and lung function	Mouse	Short lead time required
		after bleomycin treatment		
Wound Healing *	N/A	Latency to heal after 8mm skin biopsy	Mouse,	Short lead time required,
-		punch	Rat	No positive control available

Urogenital:

Assay	Validating Compound	Parameters	Species	Comments
Micturition, Overactive Bladder, Urinary Incontinence*	Oxybutynin	Urinary latency, frequency, and volume	Mouse, Rat	Short lead time required, Good reproducibility

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Assay	Validating Compound	Parameters	Species	Comments
Conditioned Place Preference	Morphine, Oxycodone,	Preference Score (seconds)	Mouse,	Variable duration depending upon
	(-) Pentazocine		Rat	training paradigm selected
Drug Discrimination	Amphetamine	Response rate (lever press)	Mouse,	Variable duration depending upon
			Rat	training paradigm selected
Locomotor Sensitization	Amphetamine,	Locomotor activity following drug	Mouse,	An early indicator or abuse liability
	Nicotine/Varenicline	administration over a 2-week period	Rat	
Self-Administration	Morphine	Rate of self-administration events	Mouse,	A gold standard model of abuse
		following a training period	Rat	potential,
				Longer duration required for training
				paradigm
Withdrawal/Dependence	N/A	Withdrawal syndrome (teeth	Mouse,	Can be combined with Irwin assay
		chatter, yawns, shakes/tremors,	Rat	
		abdominal writhes/gasps),		
		Changes in systolic/diastolic blood		
		pressure, heart rate		

Drug Abuse and Addiction:

General Safety Assessment:

Assay	Validating Compound	Parameters	Species	Comments
<u>Histology</u>	N/A	Histology evaluation, immunohistochemistry staining, pathology scoring, cell counting, FACS analysis	Mouse, Rat	Histology services in collaboration with CaresBio Laboratory
Irwin *	Diazepam	Clinical evaluation of neurobiological and physiological parameters	Mouse, Rat	Can be used as safety pharmacology assay or to interpret other responses
<u>Open-Field Activity *</u>	Risperidone	Locomotor parameters in an automated open field	Mouse, Rat	Typically coupled with other assays, Short lead time required, Good reproducibility
Pharmacokinetics	N/A	Volume of distribution, half-life, total drug exposure, clearance, oral bioavailability and Cmax, trough drug plasma levels	Mouse, Rat	Useful for drug exposure, pharmacokinetic modelling, prediction of dose requirements, assess bioavailability/bioequivalence
Rotarod *	Haloperidol	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay





Pharmacokinetics/Pharmacodynamics:

Assay	Validating Compound	Parameters	Species	Comments
Bioanalysis	N/A	Small molecule concentrations	Mouse,	Bioanalysis services in collaboration
			Rat	with Keystone Bioanalytical
Pharmacokinetics	N/A	Volume of distribution, half-life,	Mouse,	Useful for drug exposure,
		total drug exposure, clearance, oral	Rat	pharmacokinetic modelling,
		bioavailability and Cmax, trough		prediction of dose requirements,
		drug plasma levels		assess bioavailability/bioequivalence
Receptor Occupancy	Buprenorphine,	Interaction of drug candidates with	Mouse,	Typical group size: n=4
	Naloxone	their targets in the brain	Rat	

Seizure Potential:

Assay	Validating Compound	Parameters	Species	Comments
6-Hz Psychomotor Seizure	Valproate	Seizure exhibition	Mouse	Epilepsy
				Fast turn-around time,
				Good reproducibility
Audiogenic Seizure/FMR1	R-baclofen	Locomotor activity,	Mouse	Fragile X Model
Knockout		Seizure (score 0-4)		Short lead time required,
				Good reproducibility
Lithium Pilocarpine Status	Diazepam,	Cortical EEG activity in response to	Rat	CNS/Epilepsy,
<u>Epilepticus</u>	Pilocarpine	pilocarpine-induced SE		Short lead time required,
				Good reproducibility
Pro- and Anti-Convulsant Evaluation	Diazepam,	Sub-clinical seizure threshold in	Mouse,	Highly specialized capability
	Pentylenetetrazol	response to seizure-inducing agents	Rat	
Pentylenetetrazol-Induced Seizures *	Diazepam	Time to initial colonic seizure,	Mouse,	CNS/Epilepsy,
		Time to initial tonic seizure,	Rat	Short lead time required,
		EEG measurements		Good reproducibility
Maximal Electroshock *	Phenytoin	Seizure (presence/absence)	Mouse	6 Hz seizure,
				Short lead time required,
				Good reproducibility