Melior Discovery, Inc.

Word-Class Preclinical *In Vivo* Pharmacology

Pioneer in Drug Repositioning and *In Vivo* Phenotypic Screening

COMPANY OVERVIEW AND SERVICES OFFERED

APRIL 2025

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1. EXECUTIVE SUMMARY

1.1 Company Overview

Founded in 2005 and based in Exton, Pennsylvania, Melior Discovery ("Melior") is a Contract Research Organization ("CRO"), offering best-in-class *in vivo* pharmacology services to the pharmaceutical, biotechnology industries and academia. Throughout the years, the Company has achieved continued success and garnered a solid reputation in the industry as a leader in drug repositioning and a pioneer of *in vivo* phenotypic screening. From such unparalleled expertise and by amassing a tremendous amount of knowledge, Melior has expanded its value-added services business and developed three unique proprietary platforms. With these platforms, a significant experience in pharmacology and a mission of helping its most demanding clients in finding new usage for existing drugs, all in a cost-effective way, and at a rapid pace, the Company has become a preferred CRO of a diversified customer base. Melior operates out of a modern animal facility comprised of over 35 full-time employees and a management team with a combined 150 years of experience in drug discovery and development. Melior aims at being a premier organization that is proactive and nimble in delivering first class *in vivo* pharmacology services in a variety of therapeutic areas, while disrupting the traditional drug discovery model with its platforms, as an alternative and a complement to the more conventional hypothesis-driven method.

1.2 Facility Overview

Melior's current, 22,094-sq. ft., BSL-2 facility is a modern, well-equipped facility located in the suburbs of Philadelphia. The AAALAC-accredited, DEA-licensed and OLAW-assured facility is divided into five distinct areas in addition to the office space and includes:

- The Vivarium, a single 1,200 sq. ft. animal holding area centrally located within the secure laboratory area, hosts 14 Thoren individually ventilated caging racks. The facility has capacity for 7,328 mice and 2,160 rats with average daily occupancy of approximately 2,100 mice and 1,300 rats.
- The Procedure Rooms (6,000 sq. ft.) count around 33 multi-use, shared rooms which are used for survival and terminal procedures and include behavioral chambers, the dual energy X-ray absorptiometry scan room, the surgery room and necropsy suite and cell culture room. Seventeen of these rooms are supplied with CO_2 via wall-mounted ports, suitable for necropsy procedures as well as supply for cell culture incubators. Nineteen of these rooms are supplied with an O_2N_2 gas mix via wall-mounted ports, that is used with isoflurane anesthesia procedures.
- The Special Housing Rooms (500 sq. ft.) which are equipped as conventional static housing areas and are used for studies requiring quarantining, hazard containment or overnight data collection (sleep or metabolic). They can also be used as Procedure Rooms.
- The Barrier Room (450 sq ft) is supplied with HEPA-filtered, UV-treated, air supply and is positively pressured relative to surrounding areas. The room holds 3 Innovive ventilated caging racks that accommodates disposable cages. The air supply to these cages is further HEPA-filtered. The room is accessed through an anti-room which is equipped with a UV-irradiation system suitable for sterilizing equipment and supplies that will enter the Barrier Room. This room is used to house immune-compromised animals that are used for Melior's xenograft oncology studies.
- A cell culture laboratory (300 sq ft) has an UV-irradiation system suitable for sterilizing all work surfaces. In addition, the room is equipped with 2 CO_2 cell culture incubators used to culture mammalian cells including human tumor cells lines. The incubators are supplied by the "house" in wall CO_2 supply described above. The room is also equipped with a 6 ft biosafety hood and an IVIS imaging system used for bioluminescent imaging of cells and mice.
- The three Wet Labs (1,000 sq. ft) which are used for analytical and experimental work. They also have contained specialized storage for controlled substances products, flammable or hazardous materials.

2. COMPANY HIGHLIGHTS

- **An established leader in drug repositioning and a pioneer in phenotypic screening.** Finding new therapies in a cost-effective manner and at a rapid pace has been Melior's goal for over 18 years. With its best-in-class, proprietary, "high throughput" phenotypic screening platform (*thera*TRACE®), Melior provides high quality, highly translatable *in vivo* pharmacology data with the capabilities to identify new drug candidates at a success rate of 30%.

- **Highly regarded *In Vivo* Pharmacology CRO with superior animal testing capabilities.** Melior is a nimble and results-oriented Contract Research Organization providing a comprehensive set of pharmacology services. The Company's impressive track record of having performed thousands of studies and evaluated hundreds of compounds has enabled Melior to build a strong reputation and consistently win new business.

- **Experienced, industry-seasoned management team.** Melior's management team has implemented a culture of excellence and a best practices approach through a lean operation from animal holding to the development of over 100 validated animal models (rats and mice) across 14 therapeutic areas. Management is supported by a highly talented team of investigators and scientists.

- **Unwavering commitment to quality and a history of strong regulatory compliance.** Melior maintains a robust quality system and strict adherence to regulations. This is evidenced by the Company's AAALAC accreditation and by customer audits.

3. PHARMACOLOGY AND ANIMAL FACILITY

3.1 Facility Overview

Melior's current 22,094-sq. ft., BSL-2 facility is located in an industrial zone at 860 Springdale Drive, Exton, PA, U.S.A., near the Lincoln Highway and forty-five minutes from Philadelphia International Airport.

Melior moved to this site in June 2006. At the time it was only a 8,116-sq. ft. facility. Prior to that, the building was mostly unfinished shell space, that Melior specifically customized for its use. In 2008, Melior expanded into an additional 5,394-sq.ft. of space. In November 2020 the Company added an additional 4,689 sq.ft. In January 2023 the Company added an additional 3,895 sq. ft.

: Outside View of the Facility

Melior conducts its *in vivo* pharmacology work from a best in class, well-equipped single-floor facility. The facility includes:

- The Vivarium, which is equipped with Thoren filter racks for housing rats and mice.
- The Procedure Rooms which are used for surgery and diagnostic testing.
- The Special Housing Rooms, which are equipped as conventional static housing areas and are used for studies requiring quarantining, hazard containment or overnight data collection.
- A Barrier Room which is equipped to house immune-compromised rodents
- The Wet Labs which are used for analytical and experimental work.

3.2 Vivarium

Caging Racks and Cash Washer

The animal facility is managed and maintained by a Vivarium Manager and staff, with support from research investigators. Oversight of the facility and program is through an Institutional Animal Care and Use Committee (IACUC) and one on-call veterinarian.

Example Procedure Rooms

3.3 Procedure Rooms

Melior's facility boasts 33 multi-use, shared rooms that are used for survival and terminal procedures with rats and mice and totaling 6,000 sq. ft.
With this number of rooms Melior is able to schedule and perform many complimentary procedures in parallel thereby reducing lead time for our clients and maximize in facility efficiency.

Example Specialty Housing Rooms

3.4 Specialty Housing Rooms

Some of the more specialized types of studies that Melior performs involved dedicated housing rooms with customized lighting schedules, for example, or isolation away from the general colony as when the study involves infection with influenza for example. Melior is able to accommodate these sorts of demands with 4 specialized housing rooms for these types of purposes.
These rooms also include sleep chambers which are located outside of the main vivarium, with environmental parameters similar to the main vivarium and with access to the rooms limited only to trained personnel conducting the study.

3.5 Wet Laboratories

Wet Laboratory

Melior has three Wet Laboratories, totaling over 1,000 sq.ft. The Company performs a wide range of analytical work, such as compound formulation, clinical chemistry analysis, ELISAs, Western blots, and a range of assays requiring such instrumentation as spectrophotometry and fluorometric measurements.

3.6 Substance Management

Controlled Substances

Melior has Drug Enforcement Agency (DEA) licenses that allow documented ordering and storing of substances classified as Schedule I, II, III, IV and V. The most recent DEA inspection was conducted in December, 2018 with no non-compliant items noted.
Controlled substances products are located in a card-key accessible cabinet that provides access to only authorized personal and records who accessed the cabinet and at what times. Non-controlled substances and Veterinary drugs are stored in the wet labs, under appropriate temperature.

Hazardous Materials

Flammable or hazardous materials such as carcinogens, toxic chemicals, mutagens/repro-toxins/teratogens, neurotoxic chemicals, detergents, disinfectants are stored in a secure and separate area. One of Melior's procedure rooms is also equipped with a chemical safety hood which is vented to the outside.

Animal Supplies

Melior stores its animal feed in the food storage room, which is set to 70°F and is supplied with humidity control

3.7 Facility Utilities and Technology

HVAC System:

Melior has a well-maintained and robust heating, ventilation and air conditioning (HVAC) system.
The entire facility, including the vivarium, uses standard constant-volume HVAC units to provide temperature, humidity, and pressure control. The air handling system uses 100% outside air and supply and exhaust flows are calibrated to provide negative pressure relative to areas outside the laboratory. The ventilation in the animal holding room supplies at least 14 air changes/hour. In most instances, ventilated racks are used in the animal holding room. These racks supply at least 70 air changes per hour to each cage. The air supply entering and leaving the cage is HEPA filtered.

A Radius System environmental monitoring system is used to continuously monitor the vivarium environmental parameters of temperature and humidity. Parameters are set as follows: humidity, 30-70% and temperature, 65-80°F with optimal temperature at 72°F.

Back-up generator:

A Baldor 60Kw 208/120v diesel back-up generator is on the premises. All HVAC units are connected to back-up power, as well as emergency lighting, security system, laboratory refrigerators/freezers and computer systems. The back-up generator is run weekly to assure appropriate functioning.

3.8 Informatics and IT Capabilities

Melior's IT system and central server are protected from the outside with a Cisco firewall. Melior's server power supply is protected with an uninterrupted power supply (UPS) and back-up generator. Protective measures against physical access to Melior's IT system and laboratories include a number of security systems such as activity monitors, door movement alarms and glass break detectors, key card access and recorded video surveillance. The Company uses a CRM for business development and project management.

3.9 Quality Systems and Regulatory

Melior maintains a solid reputation for quality. Melior's animal housing SOPs are based on the IACUC Guide and include considerations for social housing, enrichment, and bedding selection. SOPs for animal handling, dosing, blood collection and euthanasia, as well as other pertinent company SOPs are also available.

The IACUC meets on a semi-annual basis to review the animal care and use program. These meetings also include facility and laboratory inspections. The IACUC committee also meets at other times of the year to review and approve new protocols as they are submitted. Melior is also audited by its Pharma clients, although the frequency of these audits has diminished since the Company received its AAALAC (Association for Assessment and Accreditation of Laboratory Animal Care International) accreditation. The most recent AAALAC inspection was September, 2023 with no non-compliant items noted. Melior's AAALAC accreditation number is: 001687; Issued June 27, 2017.

Melior has an Office of Laboratory Animal Welfare (OLAW; with the US National Institute of Health) Letter of Assurance. Its assurance number is: ID: D16-00908, Legacy #A4717-01 valid through December 31, 2026.

As of Q422 Melior has a dedicated Compliance coordinator whose role it is to ensure that IACUC protocols and standards as well as communications with AAALAC and OLAW are maintained.

3.10 Policy on Animal Welfare

The animal care and use program is essential to the success of Melior. It is managed in accordance with the tenet that comfortable, healthy, and nutritionally appropriate animals kept under optimal environmental conditions are more likely to yield fruitful results, and in compliance with the IACUC Guide, all federal, state, and local laws and accreditations.

Melior's policy on animal welfare follows the IACUC Guide, the Office of Laboratory Animal Welfare (OLAW) principles and the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS) policy for all animals. Melior has an experienced, ACLAM (American College of Laboratory Animal Medicine) Board Certified laboratory animal veterinarian on call who performs regular visits, inspections and training sessions as part of Melior's Animal Welfare program.

As of Q422 Melior has a dedicated Compliance coordinator who role it is to ensure that IACUC compliance and training standards are maintained.

3.11 Occupational Health and Safety

Melior maintains a culture with a high regard to safe operations. The health of the Company's employees, safety of the procedures and animal handling and protection of the environment are core focuses for all projects. Adequate training and proper SOPs covering Environmental Health and Safety procedures for ensuring the safety of all animals and personnel while working at Melior has proven to reduce risks.

As of Q422 Melior has a dedicated Compliance coordinator who role it is to ensure that safety protocols, training and provision of personal protective equipment (PPE) is maintained.

4. SERVICES

4.1 Overview

Melior is a world class provider of *in vivo* pharmacology services. The Company evaluates candidate therapeutics in animal models of human disease and has performed since inception thousands of studies and evaluated hundreds of compounds. Melior's expertise, skill level, and the quality of the data produced are widely recognized by scientists throughout the global pharmaceutical and biopharmaceutical industry.

More than just a provider of *in vivo* pharmacology services, Melior is a pioneer of *in vivo* phenotypic screening and a leader in the area of drug repositioning. The Company has developed a proprietary platform, *thera*TRACE®, that enables rapid and cost-effective identification of new therapeutic potential by systematically screening candidates across an array of validated *in vivo* disease models across a broad range of therapeutic indications. This platform enables Melior to provide bespoke studies and create a solid partnership with its clients.

4.2 General *In Vivo* Pharmacology Services

Melior provides a comprehensive range of *in vivo* pharmacology services:

Pharmacokinetics:
Pharmacology is the study of the interactions between drugs and the living organism. The two main components of pharmacology are pharmacokinetics and pharmacodynamics. Pharmacokinetics (PK) refers to the movement of drugs through the body (adsorption, distribution, excretion and metabolism). Pharmacodynamics (PD) refers to the body's biological response to drugs (behavior, receptor occupancy, qEEG and other biomarkers).

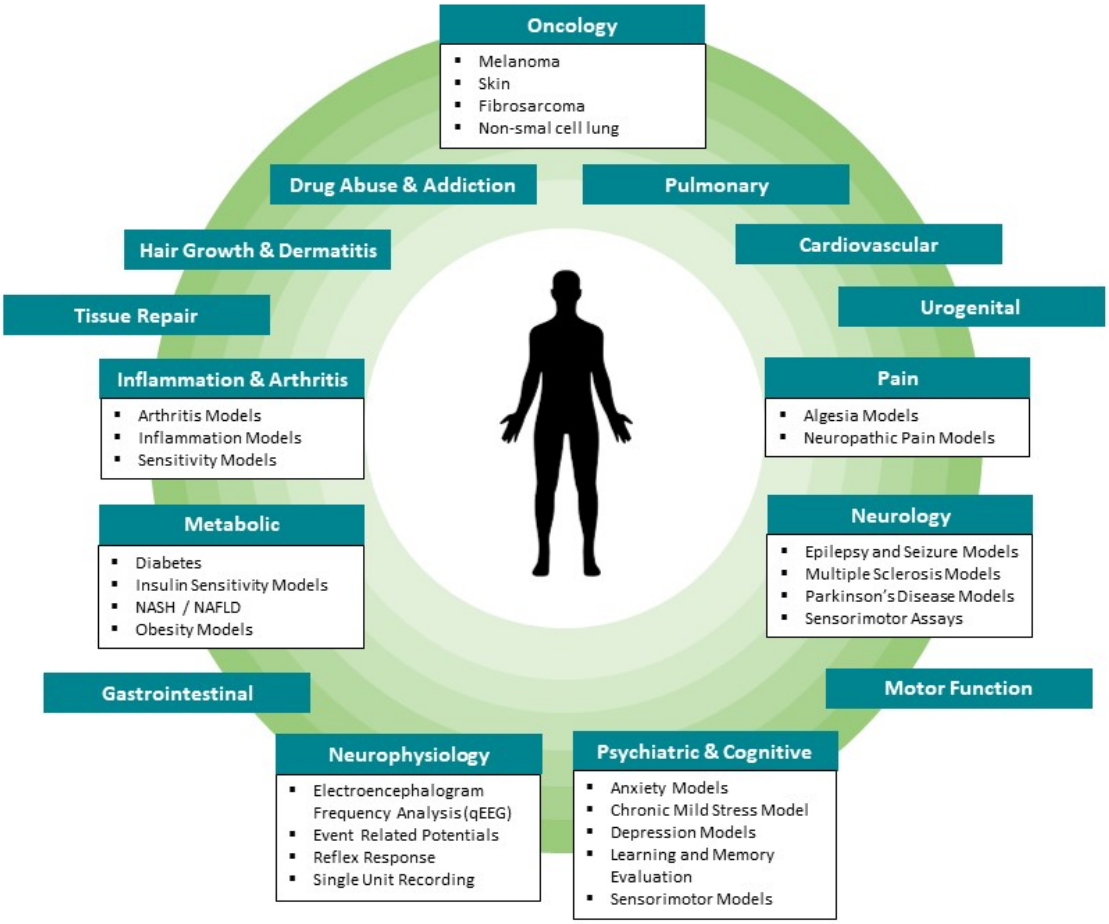
Melior customarily accompanies many of its animal model studies with PK analysis to get a more complete picture of the PK-PD relationship. Melior provides studies to address all aspects of PK and PD, including *in vivo* dosing via all routes, tissue and blood/plasma collection, bioanalysis, non-GLP noncompartmental analyses, etc. These studies are useful for drug exposure, Pharmacokinetic modelling, prediction of dose requirements and assessment of bioavailability/bioequivalence.

Bioanalysis:
Bioanalysis capabilities allow for quantitation of small molecule concentrations (e.g. drug levels) in biological samples (e.g. blood) using HPLC with tandem mass spectroscopy (LC/MS/MS). Several sample types being handled include brain, whole blood or plasma, cerebrospinal fluid or peripheral organs.

Melior offers bioanalysis services in collaboration with its partner, Keystone Bioanalytical (North Wales, PA). Melior has been working with Keystone since inception in 2005. The Company is a chosen partner because of its high reliability, fast turnaround, and reasonable cost. Melior works with Keystone as a subcontracted service to provide the bioanalytical components of a study in a turnkey solution to Melior's clients. All bioanalytical data is integrated into Melior's final study reports.

4.3 *In Vivo* Disease Models

Melior's suite of *in vivo* pharmacology services includes a wide array of *in vivo* models with broad therapeutic coverage. These include more than 90 validated animal models (both rat and mouse) across 14 therapeutic areas. These are the Company's core models but many of the studies that Melior runs for clients involve customized models or modifications of existing models.



See Appendix 2 For a complete listing of all of Melior's validated disease models

4.4 *In Vivo* Pharmacology Proprietary *Platforms*

Melior's core competency lies in its unique *in vivo* pharmacology platforms: *thera*TRACE®, *opioid*TRACE®, and *immune-thera*TRACE®. These are built on Melior's know-how around multiplexing animal models of disease--the use of a cohort of animals that might otherwise be used in a single model for multiple models without compromising data quality. This was a founding achievement for Melior in connection with its drug repositioning mission in 2005 and continues to be a unique and in-demand capability. Melior's *in vivo* pharmacology platforms are part of its extensive suite of *in vivo* pharmacology services.

The *thera*TRACE® platform: An Optimized Indications Discovery Platform

Biology is complex, and there is a tremendous amount that is not understood relying on molecular target information alone. Phenotypic screening provides a more complete understanding of the biology of molecular targets. The *thera*TRACE® platform is the Company's phenotypic screening tool for drug repositioning, drug repurposing, and indications discovery. The platform default configuration is comprised of 40 animal models spanning over 12 therapeutic areas (including Immunology, Allergy & Respiratory, Inflammation, Obesity, Diabetes, Gastrointestinal, Urology, Pain, Psychotherapeutics, Neurodegeneration, Cardiovascular, Dermatology), aimed at identifying otherwise truly unpredicted new therapeutic applications of a compound. Although the default configuration is 40 models, the platform is highly customizable and essentially all of Melior's engagements involve some level of bespoke configuration.

The *thera*TRACE® platform is comprised of a multiplexed arrangement of clinically translatable animal models. The multiplexing aspect refers to the fact that more than one assay can be performed in the same group of animals. From a scientific standpoint, the multiplexed multi-assay format has been

validated such that the particular determined arrangement of animal models responds as they would in an independent setting without compromise to the quality of the data. The practice of querying multiple models in the same animal strengthens the informative power by providing a more comprehensive analysis of the therapeutic potential of a test compound. The obvious benefit in this study design as it relates to the 3Rs (Replace, Reduce, and Refine) is that this format significantly reduces the number of animals that are required to answer the scientific questions. In addition, years of experience have allowed Melior to multiplex the models, thereby allowing this work to be done for a fraction of the cost compared to running the models independent of one another, yet without compromising the quality of the models in any way.

The Company to date has analyzed over 300 compounds in full *thera*TRACE® for its clients and over 1,000 compounds in partial platform or individual models. Key observations with *thera*TRACE® have shown that 30% of compounds profiled show new beneficial biology while up to 90% of new indications are driven by "on-target" activities. It takes 10 weeks for the platform to analyze a compound with a throughput of > 100 compounds/year (> 1,000 compounds/year through partial platforms).

See Appendix 1 For a listing of models that Melior customarily incorporates into its theraTRACE® platform

The *opioid*TRACE® platform: Analgesic Profiling

OpioidTRACE® is an *in vivo* pharmacology platform specifically tailored to the field of analgesic therapy research aimed at finding analgesic alternatives to opioid(s) with reduced liability. It examines both acute and chronic aspects of analgesia, different pain pathways, as well as respiratory depression, gastric motility and abuse liability.

With Melior's wide array of validated animal models of pain, and with the heightened interest in identifying low-abuse analgesics to address the opioid crisis, Melior has configured an *in vivo* pharmacology platform aimed at specifically profiling opioid therapeutics and related analgesics.

Over the course of a few weeks Melior can provide a comprehensive pharmacological profile of an analgesic candidate describing not just its performance in animal models of pain but also its potential liability profile. The platform is fully customizable and can be configured towards a "screening mode" that is higher throughput suitable for screening advanced candidates or "full characterization mode" suitable for more in-depth analysis of a lead. Most of the models that Melior uses in this area can be performed in either rats or mice. Most importantly, given the years of experience and frequency with which Melior runs these models, the Company also provides an interpretive brief that gives important context to the data that is being received by the client.

The *immuno-thera*TRACE™ platform: Immune-Oncology Profiling

As the field of precision medicine advances, the demand for targeted and tumor-specific immune-modulating agents is increasing. Melior's *immuno-thera*TRACE™ platform, is suited to screen immune-modulating agents for their therapeutic potential across a range of tumor types.

Immune checkpoint inhibitors (ICIs) have revolutionized cancer treatment by leveraging T-cell-based antitumor immunity. However, to effectively evaluate an immunotherapeutic agent as an antitumor agent, it needs to be tested the context of an intact immune system (i.e. not in cell culture). By developing a study design incorporating multiple syngeneic mouse models, Melior is able to determine which tumor type a therapeutic candidate is most effective against.

"Cold tumors," characterized by the absence of T-cell infiltration, show poor ICI response rates due to multiple mechanisms mediating T-cell exclusion. Several approaches have been shown to improve the efficacy of ICIs by "firing-up" cold tumors and driving T-cell infiltration.

*Immuno-thera*TRACE™ can screen immune-modulating agents, including ICIs, across various tumor types that range from hot to cold.

5. ORGANIZATIONAL STRUCTURE & STAFF

Melior currently has over 35 full-time employees working single shifts 7-days that keep the facilities and studies running 7-days a week, and 365 days a year. Its management combines over 150 years of experience in drug discovery and development. Prior to joining Melior, the management and staff-built core competencies and expertise by working with some of the most recognized multinational pharmaceutical companies such as Pfizer, Cephalon, GSK, Lundbeck, and AstraZeneca.

Melior is led by its Co-Founder, CEO and President Dr. Andrew Reaume. Throughout the Company's more than 18-year history, Management has contributed to Melior's organic growth and market expansion by providing the highest level of scientific expertise, a streamlined project management system, customer service and personal attention to every project.

Dr. Andrew G. Reaume, President, CEO, Co-Founder

Dr. Reaume founded Melior Discovery in 2005. Prior to starting Melior, Dr. Reaume was a Senior Business Analyst at Pfizer, Inc. in the department of genomics and proteomic sciences. While at Pfizer, he conceived of the idea to create a platform for comprehensively characterizing (phenotyping) genetically modified mice. He subsequently spearheaded the initiative to build it with a third-party collaborator by working closely with scientists throughout the global Pfizer organization and the partner company.

From 1993 to 1999 Dr. Reaume worked in R&D at Cephalon where he was principally involved in creating animal models of neurodegenerative disease and helped coordinate in-licensing opportunities.

In 2003, he received his MBA from the Wharton School of Business of the University of Pennsylvania where he graduated with honors in Entrepreneurial Management. He received his Ph.D. in genetics from the University of Connecticut in 1990.

Patty Ferrante, Chief Operating Officer

Ms. Ferrante has held a leadership role at Melior since 2007 being involved in diverse aspects of administration including finance, information technology, human resources and marketing. Since her arrival, and in her capacity of overseeing many aspects of Melior's operations, Ms. Ferrante has worked closely with Dr. Reaume in helping to formulate a comprehensive corporate strategy for the Company.

Ms. Ferrante comes to Melior with over 30 years of experience in project management, finance, customer service, and sales management. Prior to joining Melior, she held leadership roles in the transportation industry with prominent local agents for United Van Lines and Mayflower Transit.

Ms. Ferrante received her Bachelor of Arts degree in Management Marketing from Holy Family University in Philadelphia.

Dr. Weina Cong, VP of Research & Development

Dr. Cong joined Melior in 2016. She has more than 18 years of experience in metabolic diseases including diabetes, fatty liver disease, NASH and obesity and built extensive experience in fibrotic diseases especially liver fibrosis and pulmonary fibrosis.

From 2010 through 2015, Dr. Cong was a research fellow at the Metabolism Unit of Laboratory of Clinical Investigation, National Institute on Aging in the US. During the time at NIH, Dr. Cong not only gained extensive knowledge and experience on metabolic diseases, but also expanded her research scope to

neurodegenerative diseases including Alzheimer's disease, Huntington's disease, and Parkinson's disease. Neuro-endocrinology is one of her specialties.

Dr. Cong received her Ph.D. in pharmacology from the Peking Union Medical College (PUMC), China. During her Ph.D. study, she focused on the mechanisms of various metabolic diseases and gained extensive experience on multiple preclinical pharmacology models of metabolic syndrome.
Dr. Cong has authored over 20 peer-reviewed articles and multiple drug discovery patents in both China and the U.S.

Amy DiCamillo, Senior Director of Behavioral and Pain Pharmacology

Ms. DiCamillo is responsible for managing multiple research projects. She has 19 years of experience in the pharmaceutical industry and has acquired considerable expertise in preclinical drug discovery and development, mainly in CNS behavioral models.

Prior to joining Melior, Ms. DiCamillo was a Research Scientist at Cephalon where she worked in CNS biology developing *in vivo* animal models for cognition, anxiety/depression, locomotor activity, and pain.

Ms. DiCamillo received her M.S. from the West Chester University of Pennsylvania where she studied the locomotor effects of Modafinil in MPTP mice while working full-time at Cephalon. Ms. DiCamillo has authored or co-authored over 20 peer reviewed articles or scientific meeting presentations.

Dr. Hongyan Li, Director of Oncology

Dr. Li has over 30 years of experience in pharmacology. She authored 5 patents and over 50 peer-reviewed publications. She specializes in pre-clinical studies of anticancer therapies and diabetic complications prevention, focusing on pharmacodynamics, pharmacokinetics, and general pharmacological tests.

Prior to joining Melior Discovery in April 2022, Dr. Li was responsible for managing the Radiation Oncology Department and Antitumor Assessment Core Facility at Memorial Sloan-Kettering Cancer Center for over 8 years. She focused on radiation-induced immune response as well as establishing PDX (patient derived xenograft) models and orthotopic xenograft models.

Dr. Li is proficient in evaluating various anti-tumor therapies, including CAR-T, NK, antibodies, oligonucleotides, small molecules, nanoparticles, etc. In addition, she has expertise in immunological techniques such as FACS, Multiplex Cytokine Assays, immune-histochemistry, immuno-cytochemistry, and ELISA. She is also an expert in IVIS technique and had skillfully executed in vivo/in vitro imaging via bioluminescence.
Dr. Li earned her B.S. from Shanghai Medical University and Ph.D. from Peking Union Medical College, China. During her Ph.D. study, she led the R&D of Nicousamide to phase I clinical trial. She received post-doctoral training at National Institutes of Health, where she developed an ultra-sensitive, highly specific HPLC assay for measuring vitamin C levels in red blood cells and supported clinic pharmacokinetics study in cancer patients treated with vitamin C.
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Dr. Lindsey Mayes Hopfinger, Director of Immunology and Inflammation

Lindsey Mayes-Hopfinger, Ph.D. is a Senior Scientist at Melior who has expertise in inflammatory and cell death pathways. Lindsey graduated from Thomas Jefferson University with a Ph.D. in Biochemistry and Molecular Pharmacology. During her graduate training, she focused on understanding regulatory mechanisms of the NLRP3 inflammasome using peritonitis and colitis mouse models. In addition, she has extensive experience in *in vitro* cytotoxicity assays and cytokine ELISAs. Her favorite part of the scientific process is designing new experimental models to solve complex problems. In her free time, Dr. Mayes-Hopfinger enjoys doing anything creative as well as spending time with friends and family.

Dr. Karla Kretschmannova, Director of Neuroscience

Dr. Kretschmannova is the Director of Neuroscience at Melior. She has over 20 years of experience in both academic and pharmaceutical fields of research, with extensive experience in neurophysiology. She has authored or co-authored over 20 peer-reviewed articles.

Dr. Kretschmannova received her PhD in neurosciences from the Charles University in Prague, Czechia. Following her PhD, she completed post-doctoral training at the NIH, focusing on the complex interplay between function of ion channels and hormonal secretion in anterior pituitary cells, and at Tufts University, studying trafficking and targeting of GABAA receptors to the cell surface.
Prior to joining Melior Discovery in January 2023, Dr. Kretschmannova worked at PsychoGenics, Inc., where she designed and supervised client-tailored neurophysiological studies. She acquired extensive experience in neurophysiological alterations in neurodegenerative and psychiatric diseases including Alzheimer's, Huntington's, and Parkinson's diseases, ALS, autism spectrum disorders and major depressive disorder.

Dr. Vipin Arora, Director of Pharmacology

Dr. Vipin Arora has over 9 years of research experience across diverse therapeutic area space including pain, neuroscience and immuno-oncology. Over these years he has established and validated a number of *in vivo* models in the labs where he has worked. He has used these models to characterize novel compounds as well as for target identification.
Dr. Arora received his PhD in Pharmacology from Panjab University, Chandigarh, India. His Ph.D. work was focused on investigating the neuro-psychopharmacological aspects of the pain-depression dyad. Subsequently he worked at Harvard Medical School, University of Maryland, and Glenmark Pharmaceuticals Ltd and gained extensive experience on multiple preclinical pharmacology models of pain, CNS behavioral models, opioid reversal and immune-oncology.

Dr. Arora has the comprehensive understanding of principles of preclinical drug development with all aspects of behavioral pharmacology. In addition, he has experience in different rodent surgeries including the AAV Injections in different regions of brain, cytokine ELISAs, HPLC, brain/spinal cord micro-dialysis, flowcytometry and immunohistochemistry. Dr Arora is very detail-oriented, solution-focused, and an has a great ability to interact with multi-disciplinary drug discovery teams.

During his career, Dr. Vipin has authored or co-authored over 20 peer-reviewed articles or scientific meeting presentations.

He truly believes in Melior's mission and drug repositioning strategy and wants to achieve excellence in pharmacology and drug discovery at Melior Discovery.

Dr. John A. Gruner, Director of Neu rophysiology

Dr. Gruner specializes in working with clients to custom-design experiments to evaluate therapeutic efficacy in models of motoneuron disease (e.g. G93A transgenic SOD mice), neurotrauma, pain and muscle relaxation (nociceptive and proprioceptive spinal reflexes and neuromuscular function), sleep wake and general cortical function (including high-frequency EEG analysis and evoked potentials), and EEG-based pro- and anti-convulsant evaluation.

During his 19 years at Cephalon, Inc., he designed and supervised neurophysiological and pharmacological studies involving numerous disease areas, including evaluation of neuroprotection by trophic agents, free radical inhibitors, kinase inhibitors, and other compounds in neuropathy, neurodegeneration, and motor neuron disease models. He has also elucidated mechanisms of action of proprietary analgesic agents and utilized evoked potentials for evaluating functional impairment in models of cognitive disorders such as schizophrenia. Dr. Gruner built and ran Cephalon's preclinical sleep research laboratory and studied the actions of dopaminergic agents and other drugs in sleep wake and convulsant activity. He was a discovery team member for several sleep and wake enhancing and psychostimulant agents, including an H3-receptor inverse agonist (irdabisant) currently in clinical development.

Dr. Gruner received his B.A. from UCSD and Ph.D. from Purdue University, where he investigated the role of the cerebellum in motor control. As a postdoctoral fellow and later Research Asst. Professor in the Dept. of Neurosurgery at New York University, he designed stimulation systems for paralyzed muscle, was involved in experiments elucidating the role of synapsin phosphorylation in synaptic vesicle release, and carried out electrophysiological and behavioral studies to evaluate treatment efficacy using the spinal cord injury model he helped develop at NYU. Dr. Gruner is the author co-author of over 40 publications and 1 patent in various areas of neurophysiology.

Dr. Shamroop Mellela, Senior Scientist, Cardiovascular and Metabolic Disease.

Dr. Mallela earned his Ph.D. in biochemistry from the University of Fribourg, Switzerland. During this period, his research focused on identifying new ceramide synthase paralogues crucial in the sphingolipid signaling pathways, which are well-established as pivotal players in various diseases, including cancer, cardiovascular ailments, metabolic disorders, liver diseases, nephrological issues, and neurological conditions. He earned a master's degree in biotechnology from Bharathiar University, India, receiving a gold medal for his outstanding academic performance.

Before joining Melior Discovery, Dr. Mallela served as a postdoctoral research associate at the Miller School of Medicine, University of Miami, USA. His exceptional work during this time led to the prestigious American Diabetes Association (ADA) postdoctoral fellowship. His research in this role encompassed investigations into kidney diseases, both type I and type II diabetes, Alport syndrome, high content imaging for drug discovery, as well as the characterization of transgenic mice for the development of kidney disease models. Subsequently, he transitioned to Cardio-lab, where he delved into research on cardiovascular diseases, oncology, and obesity utilizing various preclinical rodent models.

Dr. Mallela possesses a wealth of expertise in a wide range of cellular, molecular, and immunological techniques. These skills include DNA, RNA, protein, and lipid extraction from cells and tissues, conducting apoptosis, viability, and cytotoxicity assays, performing ELISA assays, cloning, immunoprecipitation, immunofluorescence, immunohistochemistry, immunocytochemistry, Western blotting, qRT-PCR, FACS/Flow cytometry, microscopic imaging using fluorescent and confocal microscopes, tumor implantation, tumor size measurement, and conducting necropsies. He has authored more than 20 peer-reviewed articles and contributed to 2 book chapters.

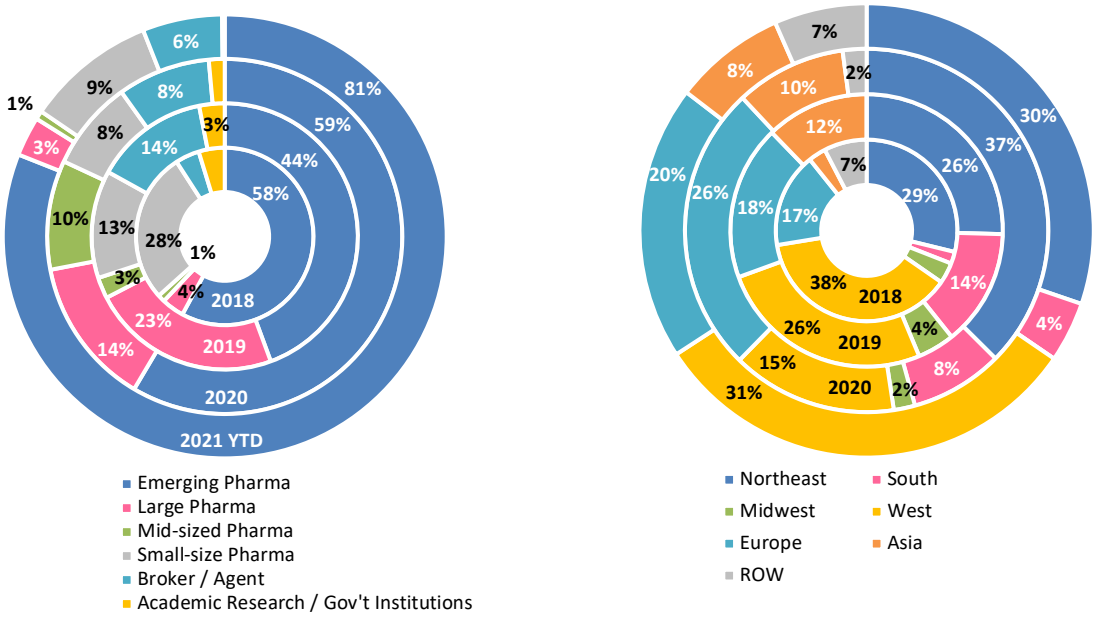
Dr. Marcia Etheridge, Attending Veterinarian

Dr. Etheridge is a consulting board certified experienced laboratory animal veterinarian (ACLAM) who visits the facility on a regular basis for IACUC meetings and to perform rounds covering all animal holding and support areas. She is involved in overseeing training of animal husbandry staff and provides her veterinary expertise in reviewing animal protocols and providing advice to investigators as they prepare new animal protocols.

6. TARGET MARKET AND CUSTOMERS

In FY 2020, Melior counts most of its customers in North America, Asia and a growing number of important customers from Europe. As per the chart below, the Company generates its revenues predominantly from Emerging Pharma companies, while keeping a strong customer base of large and mid-sized pharma who have chosen Melior as the CRO of choice for their pharmacology needs based on the Company's scientific competency and customer-centric focus.

Figure 6.3- 2018 Client Base by Revenue



Left – Breakdown per customer category **Right – Breakdown per geography**

As Top 10 customers vary year to year, around 30% of all Melior's customers are repeat during the period 2018-2021. Client satisfaction is key to not only spread favorable word-of-mouth but also to maintain repeat business from the same clients.

7. CLIENT SUCCESSES

At Melior, we recognize the requirement of product value generation towards raising additional capital or achieving an exit. We further understand that until clinical proof-of-concept data is generated, in vivo model data is usually the most important value-add that a product receives. We carefully approach every study that we conduct for clients with this in mind, and we are thrilled (vicariously) when we see our clients achieve great success, especially in the event that the data we provided played a pivotal part.

The number of our studies that have been submitted to INDs, or contributed to pitch decks that got funded, is too numerous and hard-to-track here. Therefore, over the last ten years, we have begun to assemble a sort of "best of" list comprised of companies whom we have provided data to that were subsequently purchased by a larger company. In all cases, the acquisitions came within a year or two of the studies that we completed for that client and we are delighted if our contribution was an important part of the story.

Melior Clients Acquired

Date	Client	Acquiror	Deal Value*
2016	Tolero	Sumitomo Dainippon	$580 MM
2019	NuEvolution	Amgen	$167 MM
2021	Soliton	Allergan	$550 MM
2023	Bellus	GSK	$2 Bln
2024	Modifi Biosciences	Merck	$1.3 Bln

*or potential deal value where future milestones are concerned

While all the credit for these deals undoubtedly goes to the ingenuity and hard work of these management teams; we are nonetheless so proud to be part of the value generation from these multiple exits.

APPENDIX 1

*thera*TRACE®-VALIDATED MODELS

*thera*TRACE® 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
DEXA
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

MELIOR DISCOVERY

APPENDIX 2

LIST OF VALIDATED MODELS

in vivo assay capabilities

MELIOR DISCOVERY

Cardiovascular:

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

Gastrointestinal:

Assay	Validating Compound	Parameters	Species	Comments
Colonic Propulsion *	Morphine	Latency to colonic expulsion of glass bead	Mouse, Rat	Short lead time required, Good reproducibility
DSS – Model of Colitis *	Cyclosporin A	Body Weight Gastrointestinal distress	Mouse	Short lead time required, Good reproducibility
Fecal Output *	Morphine	Fecal pellet count	Mouse, Rat	Short lead time required, Good reproducibility
Gastrointestinal Transit *	Morphine	Intestinal distance traveled of gavage – administered charcoal bolus	Mouse, Rat	Short lead time required, Good reproducibility
IBS and Acetylcholine Writhing *	Morphine	Time to writhing onset Number of writhes	Mouse, Rat	Short lead time required, Good reproducibility
Morphine-Induced Constipation *	Naloxone	Latency of colonic expulsion of glass bead	Mouse, Rat	Short lead time required, 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
Delayed – Type Hypersensitivity	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

*Models featured on *thera*TRACE® platform

in vivo assay capabilities

MELIOR DISCOVERY

Infectious Disease

Assay	Validating Compound	Parameters	Species	Comments
Influenza	Oseltamivir (Tamiflu®)	Survival, Body weight, SpO2	Mice	Can be adjusted, by inoculation titer to lethal vs. sublethal
Sepsis	Dexamethasone	TNF-(and IL-6 blood levels after lipopolysaccharide challenge	Mouse, Rat	Acute model, Short lead time required, 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
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
Capsaicin Hyperalgesia Assay	Morphine	Pain responsiveness after Capsaicin inflammation	Rat	Short lead time required, Good reproducibility
Collagen Induced Arthritis*	Dexamethasone	Clinical evaluation of paw and joint inflammation	Mouse, Rat	Strain sensitive, Short lead time required, Good reproducibility
Delayed Type Hypersensitivity*	Dexamethasone	Footpad thickness after immunogenic challenge	Mouse, Rat	Short lead time required, Good reproducibility
EAE Model of Multiple Sclerosis *	FTY 720	Clinical Scores Body weight	Mouse, Rat	Strain and supplier sensitive Good reproducibility
Formalin Analgesia Assay*	Oxycodone	Duration of Phase I (acute) pain, Duration of Phase II (delayed) pain	Mouse, Rat	Short lead time required, Good reproducibility
LPS – Pulmonary Inflammation *	Dexamethasone	Cytokine and MCP-1 levels in dissected lung tissue, Cellular infiltrate analysis	Mouse, Rat	Acute model, Short lead time required, Good reproducibility
LPS – Systemic Inflammation*	Dexamethasone	TNF-(and IL-6 blood levels after lipopolysaccharide challenge	Mouse, Rat	Acute model, Short lead time required, Good reproducibility
Monocyte Infiltration *	Dexamethasone	MCP-1 levels from peritoneal lavage, Differentials	Mouse, Rat	Short lead time required, Good reproducibility
Pulmonary Allergic Asthma*	Dexamethasone	Cytokine and MCP-1 levels in dissected lung tissue, Cellular infiltrate analysis	Mouse, Rat	*Ovalbumin:* Chronic Model, Short lead time required, Good reproducibility
Zymosan-A Induced Peritonitis	Dexamethasone	Zymosan-A induces leukocyte accumulation in the peritoneum	Mouse	Short lead time required, Good reproducibility

*Models featured on *thera*TRACE® platform

in vivo assay capabilities

MELIOR DISCOVERY

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
mHFD-Induced NASH 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

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in vivo assay capabilities

MELIOR DISCOVERY

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

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in vivo assay capabilities

MELIOR DISCOVERY

Motor Function:

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

Neurology:

Assay	Validating Compound	Parameters	Species	Comments
6-Hz Psychomotor Seizure	Valproate	Seizure exhibition	Mouse	Epilepsy Fast turn-around time, Good reproducibility
6-OHDA Lesion	Amantadine	Rotational behavior, Dopaminergic markers, Dyskinesias	Rat	Neurodegenerative symptomatic Parkinson's disease model Evaluate akinesia or dyskinesia
Audiogenic Seizure/FMR1 Knockout	R-baclofen	Locomotor activity, Seizure (score 0-4)	Mouse	Fragile X Model Short lead time required, Good reproducibility
Catalepsy *	Haloperidol	Reversal of haloperidol-induced cataleptic response	Mouse	Short lead time
Experimental Autoimmune Encephalomyelitis (EAE)	FTY 720	Clinical scores, Body weight	Mouse, Rat	Strain and supplier sensitive, Good reproducibility
EEG Pro- and Anti- Convulsant Evaluation	Diazepam, Pentylenetetrazol	Sub-clinical seizure threshold in response to seizure-inducing agents	Mouse, Rat	Highly specialized capability
L-DOPA Induced Dyskinesia	Amantadine	Axial, limb and orolingual AIMs	Rat	Neurodegenerative model of Parkinson's Disease, Short lead time required, Good reproducibility

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Lithium Pilocarpine Status Epilepticus	Diazepam, Pilocarpine	Cortical EEG activity in response to pilocarpine-induced SE	Rat	CNS/Epilepsy, 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 Disease *	L-deprenyl	Locomotor parameters in an automated open-field apparatus, Striatal dopamine levels, Dopamine cell number (TH staining; substantia nigra)	Mouse	Neurodegenerative model of Parkinson's Disease, Strain and supplier sensitive, Short lead time required, Good reproducibility
Pentylenetetrazol-Induced Seizures *	Diazepam	Time to initial colonic seizure, Time to initial tonic seizure, EEG measurements	Mouse, Rat	CNS/Epilepsy, Short lead time required, Good reproducibility
Rett Syndrome Neurodevelopment Model	N/A	Locomotor, Respiration, Seizure, Mortality	Mouse	Neurodegeneration/Rett Syndrome, Breeding limitations, Actively breeding colony
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 Electromyography (EMG)	N/A	Flexor (C-fiber), la, H reflex aptitudes	Rat	Muscle response, spasticity Highly specialized capability
Cortical EEG Frequency	N/A	Cortical EEG activity evaluated as function of frequency	Mouse, Rat	Highly specialized capability
Cortical Sensory Evoked Potentials	N/A	Cortical response to peripheral sensory stimulus	Rat	Cognitive disorders (Schizophrenia, Stroke, Head Injury), Highly specialized capability
EEG Sleep/Wake and Motor Activity	Caffeine, Modafinil, Pentobarbital	Sleep architecture, Circadian rhythm, Sleep/wake enhancement, CNS drug side-effects	Mouse, Rat	Highly specialized capability
Motor Evoked Potentials and Nerve Conduction	N/A	Nerve conduction velocity, Neuromuscular function	Rat	ALS, Motor Neuron Diseases, Highly specialized capability
Proprioceptive Spinal Reflexes	N/A	H/M response amplitude	Rat	Highly specialized capability
Pro- and Anti-Convulsant Evaluation	Diazepam, Pentylenetetrazol	Sub-clinical seizure threshold in response to seizure-inducing agents	Mouse, Rat	Highly specialized capability
Subthalamic Nucleus (STN) Recording *in vivo*	N/A	STN bursting patterns	Rat	Neurodegenerative model of Parkinson's Disease, Highly specialized capability

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MELIOR DISCOVERY

Oncology

Assay	Validating Compound	Parameters	Species	Comments
Breast: EMT6	Anti-PD-1, Paclitaxel	Tumor growth kinetics	Mouse	Subcutaneous, Orthotopic, Metastatic
Colorectal: CT26.WT	Anti-PD1, Paclitaxel	Tumor growth kinetics	Mouse	Subcutaneous, Orthotopic
Fibrosarcoma: WEHI164	Anti-PD1, Paclitaxel	Tumor growth kinetics	Mouse	Subcutaneous
Leukemia – L1210	Cyclophosphamide	Tumor growth kinetics	Mouse	Intraperitoneal, monitored by survival
Liver: Hepa1-6	Anti-PD1, Paclitaxel	Tumor growth kinetics	Mouse	Subcutaneous
Lung: LLC	Paclitaxel, Cisplatin	Tumor growth kinetics	Mouse	Subcutaneous
Melanoma: B16-F10	Anti-PD1, Paclitaxel Cisplatin	Tumor growth kinetics	Mouse	Subcutaneous, Orthotopic, Metastatic
Pancreas: KPCY	Anti-PD1, Paclitaxel	Tumor growth kinetics	Mouse	Conducted in immune competent animals
Osteosarcoma: K7M2	Anti-PD1, Cisplatin	Tumor growth kinetics	Mouse	Subcutaneous, Orthotopic
Breast: MCF7 MCF7 -Luc	Paclitaxel	Tumor growth kinetics	Human cells in mouse	Subcutaneous, Orthotopic
Colorectal: HCT-15	Cisplatin	Tumor growth kinetics	Human cells in mouse	Subcutaneous
Glioma: U87MG	Cisplatin	Tumor growth kinetics	Human cells in mouse	Subcutaneous, Orthotopic
Glioma: LN229/LN229-Luc	Cisplatin	Tumor growth kinetics	Human cells in mouse	Subcutaneous, Orthotopic
Kidney: HEK293	Cisplatin	Tumor growth kinetics	Human cells in mouse	Subcutaneous
Kidney: 786-O	Cisplatin	Tumor growth kinetics	Human cells in mouse	Subcutaneous
Liver: HepG2/HepG2-luc	Paclitaxel	Tumor growth kinetics	Human cells in mouse	Subcutaneous, Orthotopic
Lung: A549	Cisplatin, Paclitaxel	Tumor growth kinetics	Human cells in mouse	Subcutaneous
Ovary: SK-OV-3	Paclitaxel	Tumor growth kinetics	Human cells in mouse	Subcutaneous, Orthotopic
Pancreas: PANC-1		Tumor growth kinetics	Human cells in mouse	Subcutaneous, Orthotopic
Prostate: LNCap	Cisplatin	Tumor growth kinetics	Human cells in mouse	Subcutaneous, Orthotopic
Colon: Adenocarcinoma PDX		Tumor growth kinetics	Human tumor (PDX)	Consensus whole exome seq. available

in vivo assay capabilities

MELIOR DISCOVERY

Pain:

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

*Models featured on *thera*TRACE® platform

in vivo assay capabilities

MELIOR DISCOVERY

Psychiatric and Cognitive:

Assay	Validating Compound	Parameters	Species	Comments
Chronic Mild Stress – Corticosterone Levels *	Desipramine	Corticosterone levels after physical and/or immunological stress, Coupled stress-induced fecal output	Mouse, Rat	Chronic study, Good reproducibility, Group sizes n>12
Chronic Mild Stress - Stress-Induced Hyperthermia *	Diazepam	Core body temperature in response to stress	Mouse, Rat	Short lead time, Good reproducibility
Chronic Mild Stress – Tail Suspension Test	Desipramine	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	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	Group sizes n>10
Morris Water Maze	Scopolamine	Visual spatial navigation	Mouse, Rat	Short lead time required, Good reproducibility
Novel Object Recognition Test	Scopolamine	Cognition, Recognition index	Mouse, Rat	Inter-experiment variability
Open-field Activity *	Risperidone	Locomotor parameters in an automated open-field	Mouse, Rat	Typically coupled with other assays, Short lead time required, Good reproducibility
Rotarod *	Haloperidol	Coordination, Acceleration	Mouse, Rat	Primarily utilized as pharmacology safety assay
Social Recognition	Armodafinil	Short term memory, Investigation duration	Rat	Short lead time required, Good reproducibility
Startle Prepulse Inhibition *	Risperidone	Sensorimotor gating	Mouse	Short lead time required, Good reproducibility, Group sizes n>10
Stress-Induced Fecal Production *	N/A	Fecal counts after restraint stress, Coupled with corticosterone levels	Mouse, Rat	Short lead time required, Good reproducibility
Tail Suspension *	Desipramine	Duration of behavioral despair	Mouse	Short lead time required, Good reproducibility, Group size n>10
Telemetry: Home Cage Activity	N/A	Multiple home cage activities, Locomotion, Core body temperature	Mouse, Rat	Fast turn-around, Typically coupled with other assays
Vogel Water Conflict	Diazepam	Avoidance behavior to shock	Rat	Group sizes n>10

Pulmonary:

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

Tissue Repair:

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

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

General Safety Assessment:

Assay	Validating Compound	Parameters	Species	Comments
Histology	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
Open-Field Activity *	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

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Pharmacokinetics/Pharmacodynamics:

Assay	Validating Compound	Parameters	Species	Comments
Bioanalysis	N/A	Small molecule concentrations	Mouse, Rat	Bioanalysis services in collaboration with Keystone Bioanalytical
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
Receptor Occupancy	Buprenorphine, Naloxone	Interaction of drug candidates with their targets in the brain	Mouse, Rat	Typical group size: n=4

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

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