



Melior Discovery has pioneered an efficient and systematic approach to find new uses for existing drugs and drug candidates. By applying the unique multiplexed *theraTRACE*® indications discovery platform, Melior can quickly evaluate a compound in multiple, high quality *in vivo* models in order to test the molecule's potential use in a variety of therapeutic areas. In response to growing demands, we are now able to offer this same expertise applied to the design and execution of *in vivo* studies utilizing individual efficacy models.

## *theraTRACE*® Platform

Uniquely powerful approach  
to Indications Discovery

- not "hypothesis driven"
- highly predictive *functional* animal models
- "systematic serendipity"
- multiplexing know-how makes this possible

### Pentylenetetrazole (PTZ) –induced Seizure

- » Validated with known seizure attenuating drugs
- » Animals dosed with drug or vehicle prior to PTZ administration
- » Measure latency to running-bouncing clonic and tonic-hindlimb extension seizure

### Maximal Electroshock Seizure (MES)

- » Validated with known seizure attenuating drugs
- » Animals dosed with drug or vehicle prior to shock presentation
- » Measure latency to seizure and percentage of mice exhibiting seizure

### Audiogenic Seizure

- » DBA/2 mice used at early age
- » Measure percentage of mice exhibiting seizure

### Observation for Seizure Propensity

- » Mice observed for convulsions over time
- » Handling-induced convulsions (HIC) measured

### EEG Recording for Seizure Propensity

- » Based on cortical EEG recording in chronically implanted rats up to 24 h
- » Records examined for seizure-like activity according to standard criteria
- » Drug is dose-escalated until a seizure-evoking dose is observed
- » Determination of maximum tolerated dose / ED<sub>50</sub>

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