aragen.com

Integrated DMPK services for lead optimization and IND filing

Aragen's uniqueness comes from its ability to provide comprehensive DMPK expertise and technologies from the early drug discovery to lead optimization processes, and IND filing for small and large molecules. We help our customers with different mechanistic DMPK studies including *in vitro* ADME and *in vivo* PK as a part of the whole process to rank compounds, optimize their properties and to be developed from the typical efficacious hits to drug like candidates.

TIER 1 ASSAYS

- Solubility (Kinetic and Thermodynamic, SIF, SGF)
- *Log P* and *Log D*
- PAMPA (GIT, BBB and Skin)
- Metabolic stability in microsomes and hepatocytes (2 time points, Multispecies)
- Protein binding (Single concentration)
- Cocktail CYP inhibition, HLM (Single concentration, 5 CYPs)
- Cassette IV PK
- Cassette PO PK

TIER 2 ASSAYS

- Plasma protein binding (3 concentrations, 3-5 species)
- Metabolic stability (Intrinsic Clearance)
- Plasma/blood stability
- CYP Inhibition (IC50, Ki)
- Met ID (soft spot), species comparison
- Blood / plasma Partitioning
- Time dependent inhibition / Mechanism based inactivation
- Reactive metabolites
- MDCK and Caco-2 permeability
- Rat IV PO PK
- Mouse IV PO PK
- Dog IV PO PK
- Blood brain barrier penetration studies (Brain and CSF) in rodents

TIER 3 ASSAYS

- Reaction Phenotyping
- Single raising dose in rat
- Single raising dose in mouse
- Single raising dose in dog
- CYP Induction
- Tissue distribution studies
- MTD studies in rat and mouse
- Mechanistic PK studies (Biliary excretion, First pass metabolism, BAL study)
- Metabolic Characterization and Identification of *In vivo* samples

IND PACKAGE

- Bioanalytical method validation in rodent and non-rodents
- Single and multiple dose pharmacokinetics
- Dose proportionality and absolute bioavailability in mouse, rat, and dog
- Plasma protein binding in mouse, rat, dog, and human plasma
- *In vitro* CYP450 inhibition (1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 3A4/5) in human liver microsomes
- CYP induction in human hepatocytes
- *In vitro* metabolism in, mouse, dog, and human hepatic preparations
- Reaction phenotyping in recombinant CYPs or UGTs or other enzyme systems
- Mini Ames
- Contribution of P-glycoprotein (P-gp) and breast cancer resistant protein (BCRP) in limiting drug absorption or flux

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