GVK BIO
Accelerating R&D

ADME - DMPK

GVK BIO provides comprehensive, cost-effective ADME (Absorption, Distribution, Metabolism and Excretion) support across the drug discovery paradigm for evaluating and optimizing the drug-like properties of new chemical entities (NCE). Our unique expertise lies in incorporating customized innovative approaches and advanced technologies such as high throughput screening to provide decision-enabling high quality data with rapid turnaround times (TAT). We work collaboratively with our customers, providing scientific feedback and direction to advance their drug discovery programs.

TIER 1 ASSAYS (HIT TO LEAD)

- Solubility studies (Kinetic and Thermodynamic)
- Log P / Log D and pKa
- Metabolic stability in liver microsomes (Multiple species)
- Plasma protein binding (Multiple species)
- Plasma / Blood stability (Multiple species)
- PAMPA (GIT, BBB and Skin)
- CYP P450 inhibition studies for 5/8 CYP P450 isozymes
- Caco–2 / MDCK permeability studies
- Cassette IV/PO PK

TIER 2 ASSAYS (LEAD PROFILING)

- Plasma protein binding (3 concentrations, multiple species)
- Metabolic stability in liver microsomes and hepatocytes (CLint) multiple species
- CYP P450 inhibition study (IC50 / Ki)
- *In Vitro* Metabolite characterization in liver microsomes and hepatocytes: Soft spot identification and species comparison
- Blood / Plasma partitioning (multiple species)
- Time dependent inhibition / Mechanism based inactivation in liver microsomes (KI and kinact)
- Reactive metabolite(s) screening in liver microsomes/ hepatocytes
- Caco-2 or / and MDCK-MDR1 permeability study for Pgp substrate / inhibitor characterization
- Rodent and non-rodent bioavailability studies
- Blood brain barrier Penetration studies (Brain and Cerebrospinal fluid) in rodents

TIER 3 ASSAYS (LEAD OPTIMIZATION)

- Dose proportionality pharmacokinetic studies in rodents and non-rodents
- Tissue distribution studies in rodents
- Excretion / mass balance studies in rodents
- Mechanistic PK studies (Biliary excretion, First pass metabolism and Non CYP mediated metabolism)
- Characterization of metabolism pathways
- Reaction phenotyping for CYP P450, FMO's and MAO
- Metabolite identification and characterization in *In Vivo* samples
- CYP P450 induction studies: PXR, AhR and CAR transactivation assay

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- Bioanalytical method development and validation in rodent and non-rodents
- Chemical stability studies in simulated fluids – SGF and SIF
- Plasma protein binding in rodents and non-rodents
- *In Vitro* CYP450 inhibition (1A2, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, 3A4/5) in hepatic and extra-hepatic microsomes (multiple species)
- CYP induction in human hepatocytes
- *In Vitro* metabolism in rat, mouse, dog and human hepatic preparations
- Reaction Phenotyping in recombinant CYPs or UGTs or other enzyme systems
- Non-CYP enzymes mediated metabolism study
- Pgp and BCRP transporter studies using Caco-2 cell line
- Single-and multiple-dose(s) pharmacokinetics
- Dose proportionality and absolute bioavailability in rodents and non-rodents

TARGET TO HIT

Assessment of Physiochemical & *In Vitro* ADME Properties

- *In Silico* properties
- Solubility
- Log D
- Metabolic stability
- CYP inhibition

HIT TO LEAD

Optimisation of Physiochemical & Druggable Properties

- Metabolic stability
- CYP inhibition
- Permeability
  - PAMPA
  - CACO - 2
- Plasma / Tissue protein binding
- Reactive metabolite
- *In Vivo* PK (rodent)

LEAD TO CANDIDATE IDENTIFICATION

Optimisation of Druggable Properties, IVIVC, PK/PD Correlation

- Permeability
  - CACO - 2
- Plasma / Tissue proteinbinding
- Blood / Plasma partitioning
- Met id (soft spot)
- PK (non-rodent)
- PK (rodent)
- Target tissue exposure
- IVIVC, renal / biliary CL
- Mass balance
- PK/PD

CANDIDATE SELECTION

Dose Range Finding, Safety/Tox Assessment, Interspecies Scaling

- Dose range finding studies(rodents and nonrodents)
- PK/PD
- Tissue distribution Food effect
- Gender effect
- Metabolite profiling / Metabolism pathway
- Safety profiling
- Toxicokinetics
- CYP induction
- Interspecies scaling