cyprotex
AN EVOTEC COMPANY

The Leading ADME-Tox Specialists

- **Founded in 1999**
- **Flexible solutions**
- **Scientific excellence and consultancy**
- ***In vitro* and *in silico* expertise**
- **UK and USA laboratories**
- **High capacity screening with rapid turnaround**

In vitro ADME

Permeability

- Cell permeability (Caco-2, MDCK-MDR1)
- Transporter interactions (full range of regulatory transporters)
- PAMPA

Metabolism

- Metabolic stability
  - – Microsomes, hepatocytes, S9, plasma/blood, HμREL®
- Metabolite profiling and structural elucidation
- Reaction phenotyping
- CYP and non-CYP inhibition
  - – Reversible
  - – Time dependent
- CYP induction
- Nuclear receptor activation

Distribution

- Plasma protein binding
- Whole blood binding
- Brain tissue binding
- Microsomal binding
- Blood to plasma ratio

Bioanalysis & PK

- Bioanalytical method development, method transfer and method qualification
- Pharmacokinetic analysis
- Pre-formulation development

In silico Prediction

- PBPK modelling
  - – PK prediction
- QSAR/QSPR modelling
- PK/PD modelling
- Systems biology and systems pharmacology

Physicochemical Properties

- Solubility
  - – Turbidimetric
  - – Thermodynamic
- Chemical stability
- pK_a determination
- Lipophilicity
  - – logP
  - – logD

DDI Packages

- *In vitro* drug metabolism (CYP and non-CYP)
- Transporters (efflux and uptake)
- Scientific guidance and consultancy
  - – Project-specific study design
  - – Prediction of DDI risk based on regulatory recommendations
- Both screening and regulatory services
- Bioanalytical expertise

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Toxicology

Mechanistic Toxicology

- Cell viability
- Mitochondrial toxicity
- Phospholipidosis and lysosomal trapping
- Steatosis
- Apoptosis
- Reactive metabolite assessment
- 3D microtissue models
- Skin toxicity
  - Phototoxicity
  - KeratinoSens™
- Cytotoxicity screening panel
  - General cell health endpoints
- Haemolysis
- Cell signalling and cell stress
- Cell cycle and proliferation
- Lysosomal trapping
- Transcriptomics

Cardiotoxicity

- Single Ion Channels
  - hERG (I_{Kr})
  - Nav1.5
  - Kv4.3 (I_{to})
  - KvLQT1/minK (I_{Ks})
  - Cav1.2
  - kir2.1(I_{K1})
- Whole Cell Physiology
- MEA assessment of iPSC-derived cardiomyocytes (eCiphr®Cardio)
  - 3D microtissue models
  - Structural and functional cardiotoxicity

Hepatotoxicity

- CellCiphr® Premier
  - Multiple cell types, time points and endpoints
- 3D microtissue models
  - DILI
  - Cholestasis
- Transcriptomics
- Reactive metabolites
- Phospholipidosis and steatosis
- Mitochondrial toxicity

Neurotoxicity

- MEA assessment of neurons (eCiphr®Neuro)
- Neurite outgrowth
- 3D neurotoxicity

Nephrotoxicity

- Chronic exposure nephrotoxicity assay

Immunotoxicity

- PBMC cytotoxicity
- PBMC proliferation
- Dendritic cell perturbation

Genotoxicity

- Ames test
- *In vitro* micronucleus test
- GreenScreen HC™
- p53 (phospho-p53)
- pH2AX (phospho-H2AX)
- Tubulin (microtubule stability)
- GADD153

Innovations

eCiphr®Cardio

- Synchronously beating iPSC-derived cardiomyocytes
- Whole cell physiology
- High-throughput micro-electrode array (MEA)

eCiphr®Neuro

- Measure mean firing rate
- High-throughput micro-electrode array (MEA)

Transcriptomics

- Toxicology Prediction
  - Organ-specific
  - Species-specific

3D Microtissues

- Scaffold-free cultures
- Closely mimic native tissue
- Multiple dosing and extended exposure
- Liver, cardiac, brain and kidney models

CellCiphr® Premier

- Multiple cell types and time points
- Extensive range of endpoints
- Relates to exposure

PK Prediction

- Using *in vitro* ADME data
- Oral, IV bolus or infusion

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