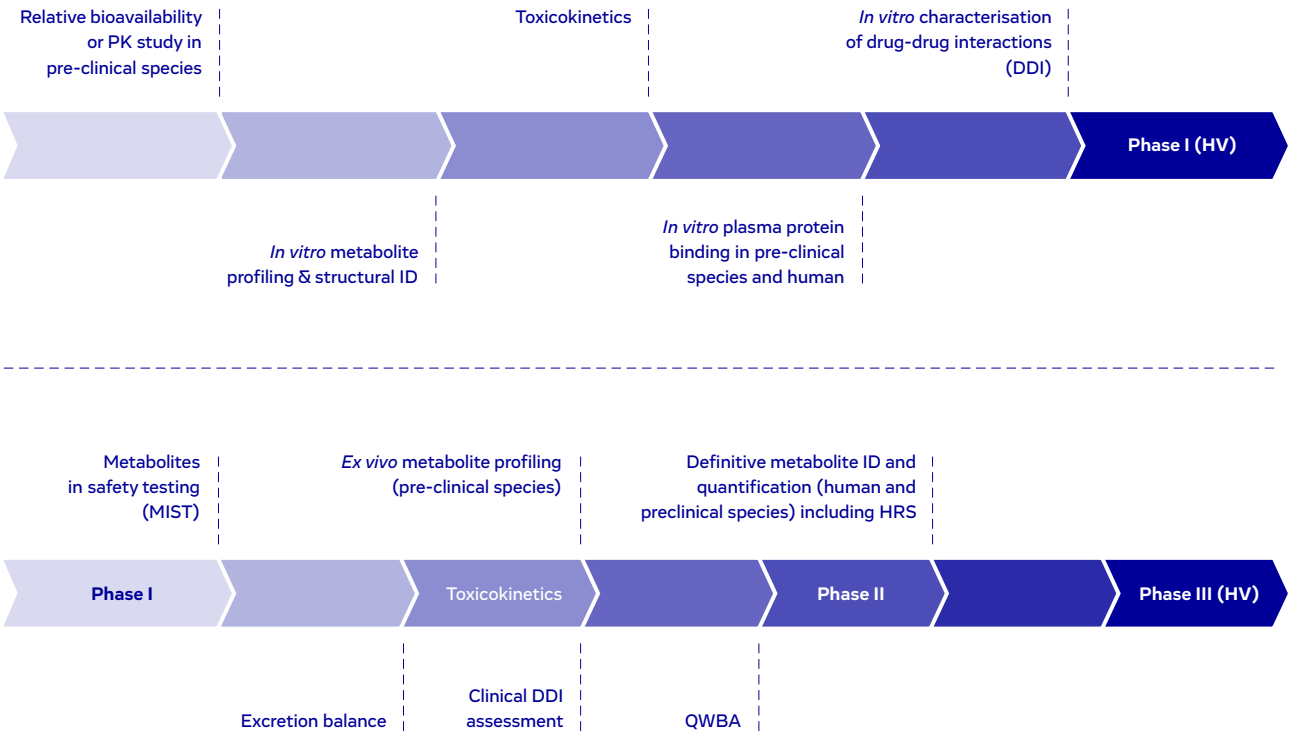
evotec

#RESEARCHNEVERSTOPS

Regulated ADMET Services

- Broad areas of expertise with a full vision through all drug development phases up to filing
- Dynamic team of expert scientists capable of handling projects of any complexity in regulated environment
- State-of-the-art labs and technologies
- Full integration with in-house bioanalytical and safety assessment groups
- Tailored studies and programs based on specific client needs

ICH M3 (R2); CHMP and FDA Guideline on DDI



Regulatory ADMET provides full support to development projects to fulfil and anticipate regulatory requirements, to investigate safety issues and to accelerate the development process.

Contact our experts

info@evotec.com | www.evotec.com

In vivo ADME

In vivo Pharmacokinetics

- Radiolabelled (^{3}H, ^{14}C) and non-radiolabelled *in vivo* PK studies
- Rodent and non-rodent species
- Non compartmental analysis using Phoenix™ WinNonlin

Excretion Balance

- Radiolabelled (^{3}H, ^{14}C)
- Rodent and non-rodent species
- Urine, faeces, bile (rat only), expired air (rodents only), carcass (rodents only)

QWBA

- Radiolabelled (^{3}H, ^{14}C)
- Rodent and non-rodent species
- Tissue distribution
- Placental transfer
- Melanin binding
- Distribution across the blood-brain barrier
- Tumour penetration
- Evaluation of dosimetry to support a human radiolabelled study

In vitro ADME

Plasma protein binding

- Rapid equilibrium dialysis, ultrafiltration, ultracentrifugation
- Human, rodent and non-rodent species

Red blood cells partitioning (Blood/plasma ratio)

- Fresh whole blood
- Human, rodent, and non-rodent species

MET ID (Radiolabelled and non-radiolabelled test item)

In vitro metabolic profiling

- Cryopreserved or fresh hepatocytes and microsomes
- Qualitative or quantitative analysis
- On-line and off-line quantitative analysis (radiolabelled)
- Structural elucidation

Ex vivo metabolic profiling and human radiolabelled studies (HRS)

- Various biological matrices from pre-clinical and clinical studies
- Qualitative or quantitative analysis
- On-line and off-line quantitative analysis (radiolabelled)

MIST (Metabolites in Safety Testing)

- Analysis of samples from clinical trials using several different approaches including definitive metabolite structural characterization by NMR

In vitro DDI

CYP-450 inhibition

- Human liver microsomes
- CYP Enzymes: 1A2, 2A6, 2B6, 2C8, 2C9, 2C19, 2D6, 3A4 and 2E1, tested with validated bioanalytical method of FDA-preferred substrates
- Direct and metabolism dependent inhibition (MDI)
- K_i, K_I and K_{inact} determination
- Mechanistic investigation

CYP-450 induction

- Nuclear receptor activation (PXR, AhR and CAR)
- Cytochrome P450 induction, designed to meet FDA and EMA guidelines
- Cytochrome P450 relative induction score

Transporter substrate and inhibition

- Efflux and uptake transporter inhibition (IC_{50})
- Efflux and uptake transporter substrate identification

UGT inhibition

- Human liver microsomes
- UGT Enzymes: 1A1, 1A3, 1A4, 1A6, 1A9, 2B7, 2B15 and 2B17, tested with validated bioanalytical method of FDA-preferred substrates
- Direct inhibition

Reaction phenotyping

- Assessment of metabolite formation substrate depletion
- Radiolabelled and non-radiolabelled test item
- Recombinant CYP/non CYP enzymes and/or human liver microsomes with chemical inhibitors
- Standard and customized study designs to support DDI strategy