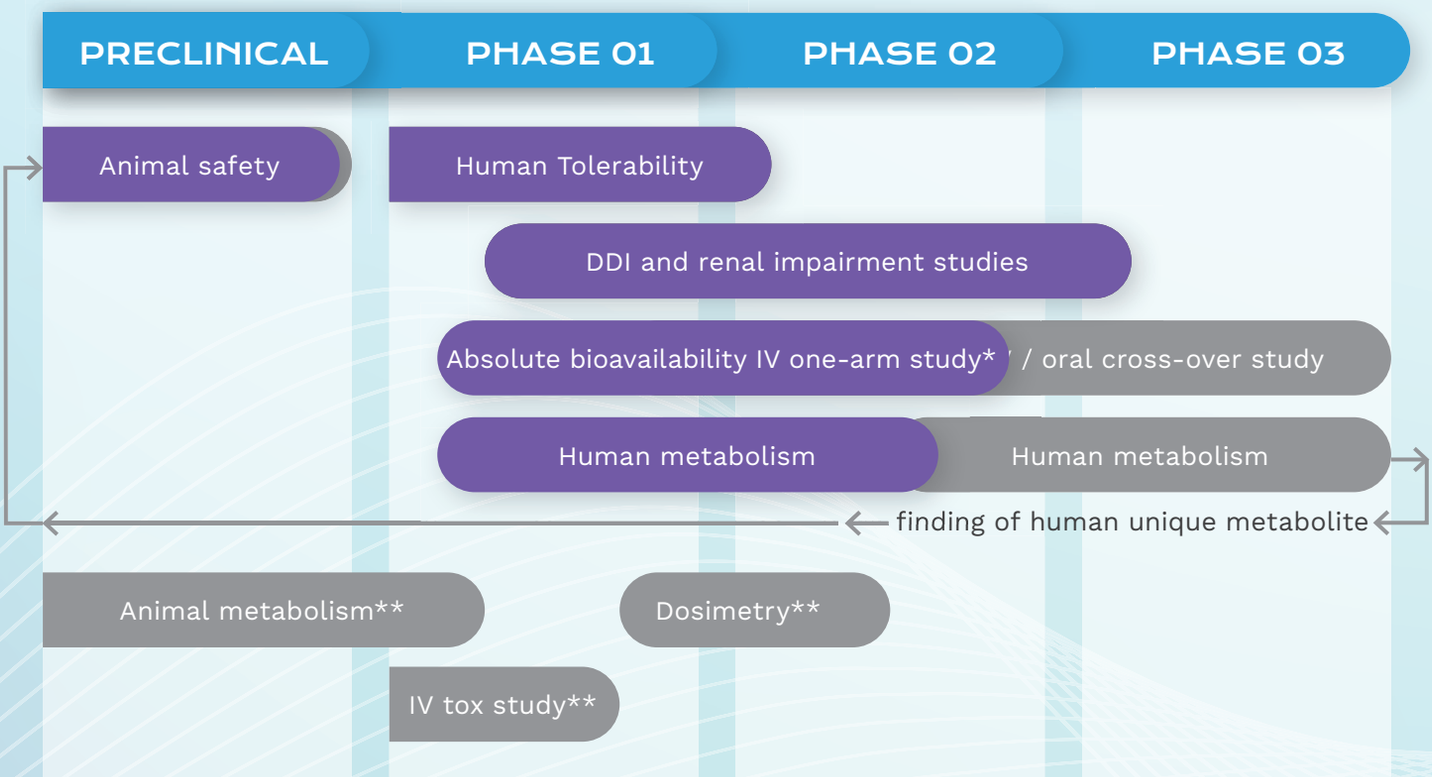
PEREGRION

Microtracer CRO for
early-stage human ADME studies

EFFICIENT ENRICHMENT OF HUMAN DATA IN EARLY-STAGE CLINICAL DEVELOPMENT

MICROTRACER STUDIES versus **CONVENTIONAL METHODS**



* With an absolute bioavailability IV one-arm study, there is no need for a second study.
** Animal metabolism and IV tox study can be waived in this workflow, and dosimetry can be pushed back.

ACCELERATE. DE-RISK. REDUCE COSTS.

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MICROTRACER STUDIES AS THE NEW STANDARD FOR HUMAN ADME

CONVENTIONAL	MICROTRACER STUDIES
• Human unique metabolites are generally found in Phase 2b/3 placing the human ADME trial on the critical path	• Human metabolite safety concerns are caught from Phase 1
• Dosimetry/QWBA is required due to Ethical Class 2 of the ICRP	• Dosimetry not required before human microtracer study
• DDI and impairment studies based on *in vitro* and *in vivo* animal data	• Early hADME data optimizes design of DDI and hepatic/renal studies
• Lack of LSC sensitivity for PK and/or metabolites in plasma of candidates with long half-life (< 100 hr)	• AMS has the required sensitivity for candidates with long half-life
• Regular dose is 100 µCi while the LSC sensitivity is ~ 0.5 Bq/LC fraction	• Microtracer dose is between 0.1 and 1 µCi (100-fold ↓) • AMS sensitivity is ~ 10 µBq/LC fraction (500-fold higher sensitivity)
• Human ADME data and AbsBA data are collected in separate studies at oral therapeutic dose	• Human ADME and AbsBA can be combined in a single cohort study due to low IV dose of ≤ 100 µg
• AbsBA is a two arm cross-over design of two-periods requiring IV toxicity data	• One arm study design is suffi cient for determination of AbsBA
• IV toxicity study is required	• No IV toxicity data is required
• Separate studies do not allow determination of fraction absorbed (Fa)	• Fraction absorbed can be determined in a two-period study
• Conducted with full GMP material, also for 14C material	• Qualifi ed 14C material often tolerated
• Animal MB/MP studies are conducted to de-risk drug development	• Early human metabolism data enables early MIST assessment
• Therapeutic dose IV formulations are complex for BCS class II and class IV with low aqueous solubility	• Microtracer dose IV formulations are generally below solubility limits
• Should always be conducted in dedicated facilities	• Possibilities for piggy-backing the microtracer on existing clinical trials
	• Complies with ALARA principle for radiation burden of participants

FDA

FDA recommendation: “Usually, sponsors have conducted human in vivo metabolism studies relatively later in drug development, but we **strongly recommend** that sponsors conduct **in vivo metabolic evaluation in humans as early as feasible**.” (FDA Safety Testing of Drug Metabolites Guidance for Industry)

Contact us for more information via info@peregrion.com or the contact page on the website