FIRST-IN-RAT™ PK

Our First-in-Rat™ PK studies are designed on our client's need to understand the IV/PO or IV/SC PK profile of a lead molecule generated from our First-in-Mouse™ PK study or from a client's own research. Upon completion of the First-in-Mouse™ study, Xyzagen recommends conducting a First-in-Rat™ study to confirm the PK in mouse and evaluate absolute bioavailability, theoretical oral bioavailability, plasma:blood compartmentalization and renal excretion.

COST: $17,000 / COST FOR PRESENTATION OF DATA BY SEX: $19,000

STUDY DESIGN (ONE COMPOUND)

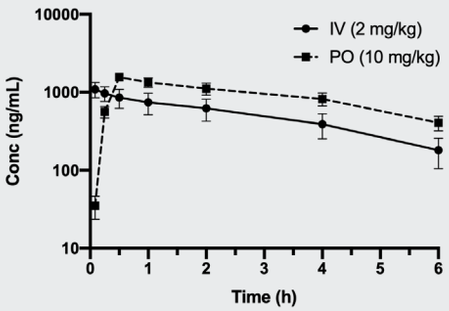
- 3 male & 3 female rats
- 275-300 g per rat; SD strain (can alter strain depending on client efficacy models)
- IV/PO or IV/SC 2 period, 2 sequence, crossover study
  - IV 4 mL/kg volume, 2 mg/kg dose, 0.5 mg/mL concentration
  - PO & SC 5 mL/kg volume, 10 mg/kg dose, 2 mg/mL concentration
  - Drug requirement: 35 mg minimum
  - 0.5% Methyl Cellulose vehicle suspension for PO & SC
  - Formulation development for IV administration
  - 200uL of blood collected
  - Full time course in each rat (2 period partial randomization with 48 h washout)
    - Period 1 plasma time points: 5, 15, 30 min, 1, 2, 4, 6, 24 h
    - Period 2 plasma time points: predose, 5, 15, 30 min, 1, 2, 4, 6, 24 h
    - Period 1 & 2 urine time periods: 0-6h, 6-24h
- Tier 2 bioanalytical method development with one compound
- Protein binding assessed at 3uM conc with N=3 replicate at 2 h on Thermo Fisher™ RED device (no positive control)

RESULTS

- Full profile PK Analysis (for each route, sex combined): AUClast, AUCinf, Cmax, MRTlast, MRTinf, %Extrap, Tmax, Tlag, T1/2; Absolute bioavailability of PO(SC) to IV based on AUClast or AUCinf. Summary tables of PK parameters and PK concentrations, body weights, clinical signs, linear and semilog Mean (SD) concentration time plots, scatter plots, spaghetti plots.
  - If >2-fold exposure difference between sex then PK and concentration presented by sex and group.
  - Renal PK parameters: Ae, renal Clearance, fe.
  - Protein binding presented as free fraction

REPORT

- PDF bookmarked report for use in IND submission or other corporate development
- Excel file of concentration time data
- Samples stored for 1 year for potential future metabolite ID



EXPERIENCED SCIENTISTS IN PHARMACOKINETIC STUDY DESIGN, IMPLEMENTATION, ANALYSIS, AND REPORTING.

Xyzagen has over 25 years of early drug discovery experience. Our lead scientists have advanced many programs from early pharmacology through Phase 2 clinical development and approval. The challenge to identify a chemical series that has pharmacological activity and is drug-able is greater with limited resources. Pharmacokinetics are critical in defining the drugability of a new chemical series. Talk to us.

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