

PHARMACOKINETICS

Small Animals

- Mouse
 - C57BL/6
 - CD-1
 - Balb/c nude
- Rat
 - SD
 - Wistar
 - Wistar Han
- Guinea pig
- Rabbit
- Gerbil
- Ferret

Aalac Accredited Animal Vivarium

- 40,000 ft² special pathogen free (SPF) rodent facility
- 18,000 ft² large animal facility
- Advanced animal care program
- Animal enrichment program

Formulation Support

- Formulation Screening
 - Pharmacology
 - Pharmacokinetics
 - Toxicology
- Solubility test in formulation under pH 3-9
- Stability test for dosing solution
- Dilution study to predict in vivo precipitation and supersaturation

Large Animals

- Mini-pig
- Canine
 - Beagle
- Non-human primates
 - Cynomolgus monkey
 - Rhesus monkey

Comprehensive *In Vivo* Techniques

- Cannulation surgery including jugular vein, portal vein, duodenum, and bile duct
- Various dosing routes including IV, PO, SC, IM, nasal, ICV, and AZ pump
- Tissue collection including spinal cord, sciatic nerve, specific brain regions, cornea, others upon request

Experienced Staff

- Founded in 2007
- 200+ scientists, 50% with MS/MD/PhD
- 10,000+ PK/PD/tox case studies and 100,000+ ADME case studies

Our Services

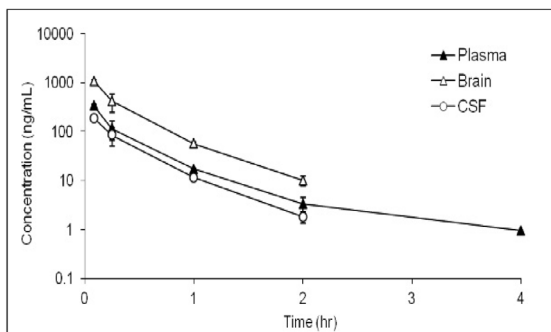
- Quality Data
 - Well established process and QC system to ensure data quality
- Fast Turnaround Time
 - 5 working days from compound receipt to data delivery for most small molecule PK
- Flexibility
 - Last minute change allowed to accommodate R&D need
- Extensive Experience
 - Over 10,000 PK studies and 150 clients globally



Extensive PK Models

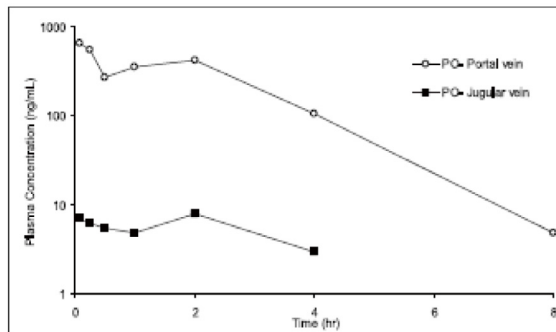
Brain Penetration Study

Mean plasma, brain and CSF concentration-time profile of CpdX after IV at 0.5 mg/kg in C57BL/6 mice



Cerebrospinal fluid (CSF) conducted can be collected in rodents and up to 7 days in mini-pig, canine and non-human primates after survival surgery.

Portal Vein Cannulation to Assess Hepatic Extraction

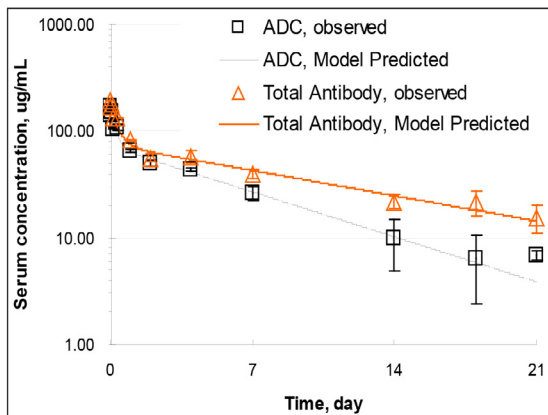


Hepatic extraction ratio estimated by
 $E (\%) = (1 - AUC_{PV} / AUC_{IV}) \times 100$

AUC_{PV}: systematic exposure via portal vein infusion
AUC_{IV}: systematic exposure via intravenous infusion

Antibody-Drug Conjugates (ADC)

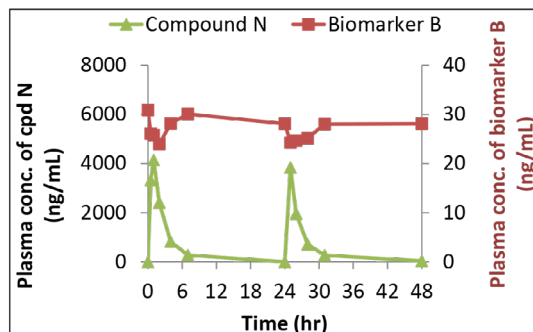
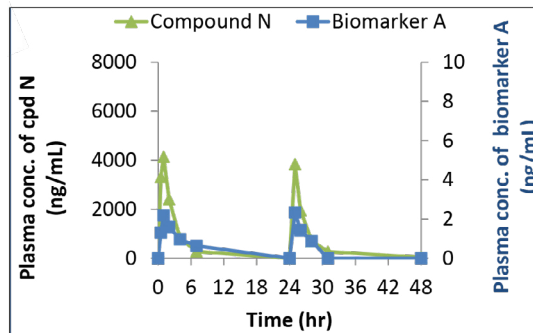
ADC PK Study in Rats



- Total antibody and ADC quantified by ELISA. Free drug analyzed by LC-MS/MS
- Free drug concentration at LLOQ (0.1 ng/mL) in systemic circulation

PK PARAMETERS	UNIT	TOTAL Ab	ADC
CL	mL/day/kg	8.23	14.7
V _{ss}	ml/kg	102	103
V ₁	ml/kg	44.3	50.6
Alpha t _{1/2}	day	0.309	0.204
Beta t _{1/2}	day	9.38	5.18

PK & PD Correlation



- PO administration of CpdN at 5 mg/kg to SD rats for two consecutive days
- Plasma levels of biomarker A and B correlate with drug concentration change