

# PHARMACOKINETICS

## SMALL ANIMALS

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

## 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

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## AAALAC ACCREDITED ANIMAL VIVARIUM

- 40,000 ft<sup>2</sup> special pathogen free (SPF) rodent facility
- 18,000 ft<sup>2</sup> 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 super-saturation

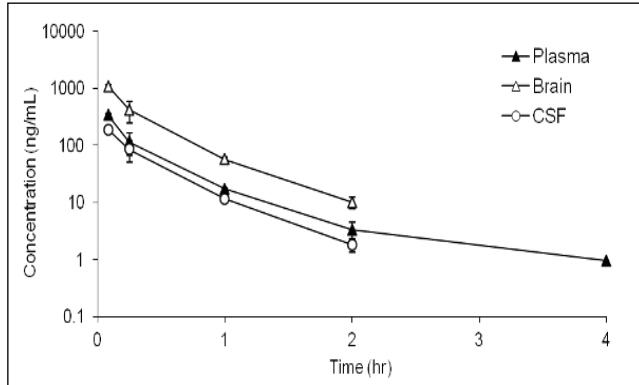
## OUR SERVICES

- 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

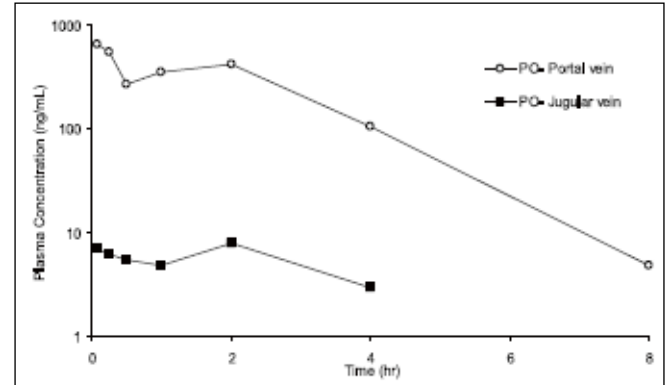
## BRAIN PENETRATION STUDY

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

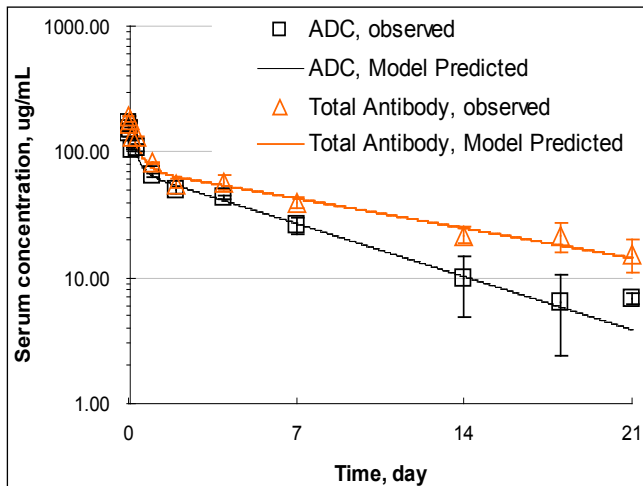


Hepatic extraction ratio estimated by  
 $E (\%) = (1 - AUC_{PV} / AUC_{IV}) \times 100$

*AUC<sub>PV</sub>*: systematic exposure via portal vein infusion  
*AUC<sub>IV</sub>*: systematic exposure via intravenous infusion

## ANTIBODY-DRUG CONJUGATES (ADC)

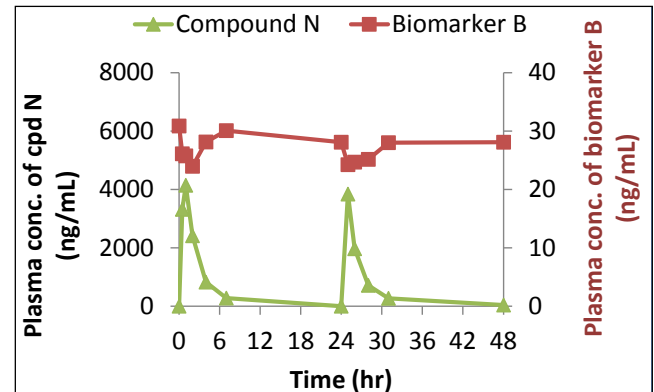
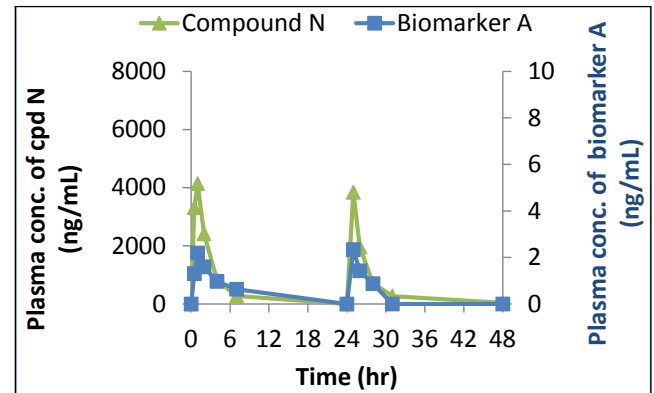
### ADC PK STUDY IN RATS



- 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 <sub>ss</sub>	ml/kg	102	103
V <sub>1</sub>	ml/kg	44.3	50.6
Alpha t <sub>1/2</sub>	day	0.309	0.204
Beta t <sub>1/2</sub>	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