

# PHARMACOKINETICS

ChemPartner's pharmacokinetics team of over 200 scientists knows that preclinical pharmacokinetics research is a vital part of drug development pipelines as it informs dosing regimens, toxicology studies, formulation development, and more. Our AAALAC and OLAW accredited animal facilities offer our clients access to broad ranges of animal species as well as state-of-the-art instruments.

## EXPERTISE

ChemPartner conducts 120-150 PK studies per week and our extensive experience includes PK model development with comprehensive *in vivo* techniques such as surgical operation and animal care.

### EXPERIENCE AND CAPABILITIES

- Founded in 2007
- 200+ scientists, 50% with MS/MD/PhD
- 10,000+ PK/PD/tox case studies and 100,000+ ADME case studies
- 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 needs
- Extensive Experience
  - Over 10,000 PK studies and 150 clients globally

### COMPREHENSIVE *IN VIVO* TECHNIQUES

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

### 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

## ANIMALS AND FACILITIES

### 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

### SMALL ANIMALS

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

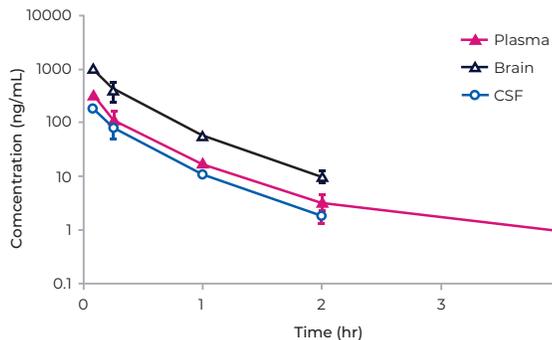
### LARGE ANIMALS

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

## EXTENSIVE PK MODELS

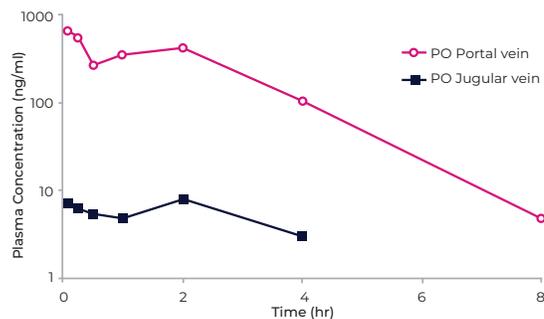
### BRAIN PENETRATION STUDY

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



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

### PORTAL VEIN CANNULATION TO ASSESS HEPATIC EXTRACTION

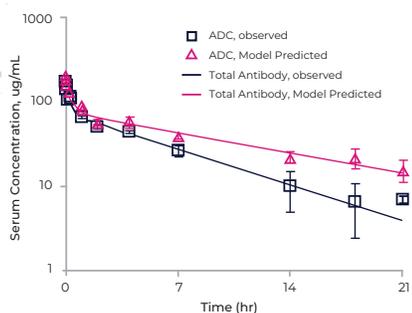


Hepatic extraction ratio estimated by  $E (\%) = (1 - AUC_{PV} / AUC_{IV}) \times 100$

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

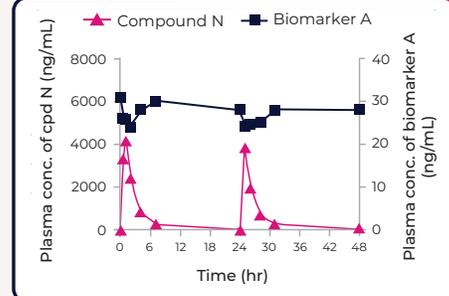
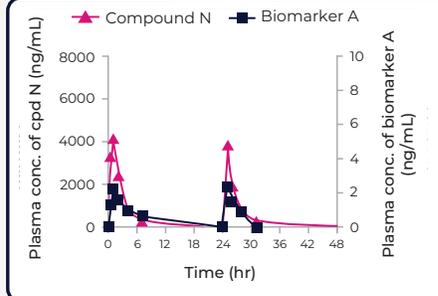
## ANTIBODY-DRUG CONJUGATES

### ADC 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 AND 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

PK PARAMETERS	UNIT	TOTAL Ab	ADC
CL	mL/day/kg	8.23	14.7
V <sub>ss</sub>	ml/kg	102	103
V <sub>I</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

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