PK/PD ANALYSIS IN RODENT MODELS

Mice and rats are typically the first models of choice for DMPK and PD studies of novel therapies. Biomere offers comprehensive PK/PD analysis in rodent models (mice and rats) to evaluate critical characteristics such as tolerability, biodistribution and adverse effects. Rodent models are an easily accessible and cost-effective solution for an initial evaluation of ADME characteristics of a new therapeutic candidate and provide valuable data to design additional PK/PD and toxicology studies.

Biomere scientists have developed deep expertise to support a broad range of PK/PD studies in rodent models including systemic and tissue-specific dosing as well as in-life and terminal sample collection and analysis. The team has experience with different drug modalities including oligos, monoclonal antibodies and derivatives such as bispecifics and ADCs, small molecules, viral vectors and nonviral gene therapy including LNPs.

DOSING ROUTES

The most common route of administration in rodent models is intravenous through the tail vein, but the Biomere team has expertise in tissue specific dosing and specialty routes of administration. Adult animals can be dosed using the following methods –

- Intravenous (IV)
- Hydrodynamic IV
- Retro-orbital
- Intraperitoneal
- Intramuscular
- Intradermal
- Intranasal
- Subcutaneous
- Oral gavage
- Direct injection into inguinal fat pad
- Intratracheal
- Intrathecal
- Unilateral and bilateral intracerebroventricular (ICV)
- Intra cisterna magna (ICM)

Neonate animals can be dosed using the following methods:

- Intravenous
- Subcutaneous
- Intraperitoneal
- Intracerebroventricular (ICV)

SAMPLE COLLECTION AND ANALYSIS

Dosed animals are monitored in-life for body weight changes and clinical observations along with blood sample collections. Extended or in-depth clinical observations are available for therapies that have been reported to cause acute adverse effects. In addition to clinical monitoring, Biomere offers fluorescent imaging (IVIS) and behavioral endpoints such as open field, rotarod and grip strength. In-life blood samples can also be analyzed using clinical chemistry panels, cytokines, serum proteins etc. as well as profile immune cells using flow cytometry panels. In addition to a growing portfolio of assays, Biomere works with partners to offer additional assays including LC-MS analysis of drug metabolites and biomarkers.

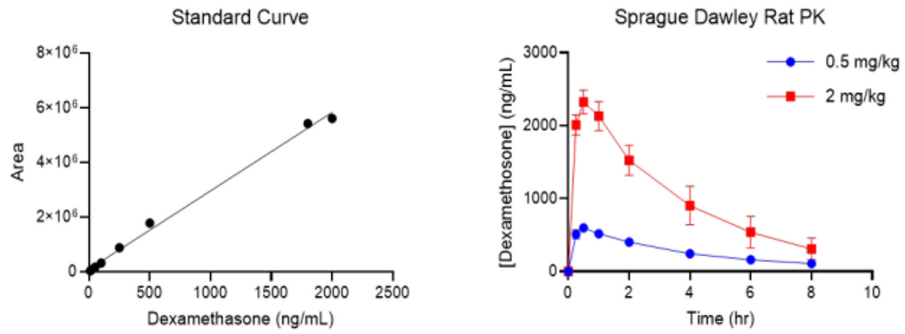

Figure 1: LC-MS analysis of plasma samples collected at specific time points from Sprague-Dawley rats dosed with 0.5 mg/kg and 2 mg/kg of dexamethasone.

Terminal collections include tissues and biofluid samples that are shipped to the client or third-party partners for downstream analysis. Biofluid collections include blood, CSF (cerebrospinal fluid) & BALF (bronchoalveolar lavage fluid). Our staff can perform microdissections including microbrain dissections and DRG (dorsal root ganglia) isolation. Tissues can be shipped frozen for mass spectrometry (LC-MS) or multiomics analysis or fixed in formalin for histopathology. In addition, Biomere is actively expanding our portfolio of endpoint assays to include readouts such as mRNA expression (q-PCR), protein expression, coagulation assays etc.