PK/PD ANALYSIS IN LARGE ANIMAL MODELS

Large animal models such as non-human primates (NHPs), rabbits and swine are typically more translational compared to rodents. NHPs, in particular, share significant anatomical, physiological and metabolic characteristics with humans and provide valuable ADME insights on novel therapies. The Biomere team has successfully completed several PK/PD, biodistribution and tolerability studies in NHPs, rabbit and swine. NHPs are versatile models for a range of systemic and tissue-specific dosing routes to the eye, CNS, immune system and cardiovascular system. NHP origin is an important consideration and Biomere has access to animals from Mauritius, China and other Asian regions. Rabbits are widely used for ocular studies due to anatomic and physiological similarities with the human eye. Additionally, the larger eye size facilitates dosing, imaging and tissue collections. Swine models such as minipigs are a model of choice for ocular and systemic PK/PD studies due to high translational potential to human conditions.

DOSING ROUTES

Large animal models are amenable to multiple systemic and tissue-specific dosing routes. Biomere scientists have expertise across multiple dosing routes in NHPs, rabbits and swine. The available routes of administration are listed below:

NHPs

- IV Bolus & Infusion
- Oral (oral gavage and tablet/capsule)
- Subcutaneous
- Intramuscular
- Intradermal
- Intranasal
- Intrathecal (direct or surgical)
- Intra Cisterna Magna (ICM)
- Intracerebroventricular (ICV)
- Subretinal (unilateral or bilateral)
- Intravitreal (unilateral or bilateral)
- Transplantation (xeno & allo)
- Surgical delivery

RABBITS

- IV Bolus
- Subcutaneous
- Intramuscular
- Subretinal (unilateral or bilateral)
- Intravitreal (unilateral or bilateral)

SWINE

- IV Bolus
- Oral (tablet/capsule)
- Subcutaneous
- Intramuscular
- Intradermal
- Subretinal (unilateral or bilateral)
- Intravitreal (unilateral or bilateral)
- Surgical delivery

Additional dosing routes can be developed in collaboration with clients.

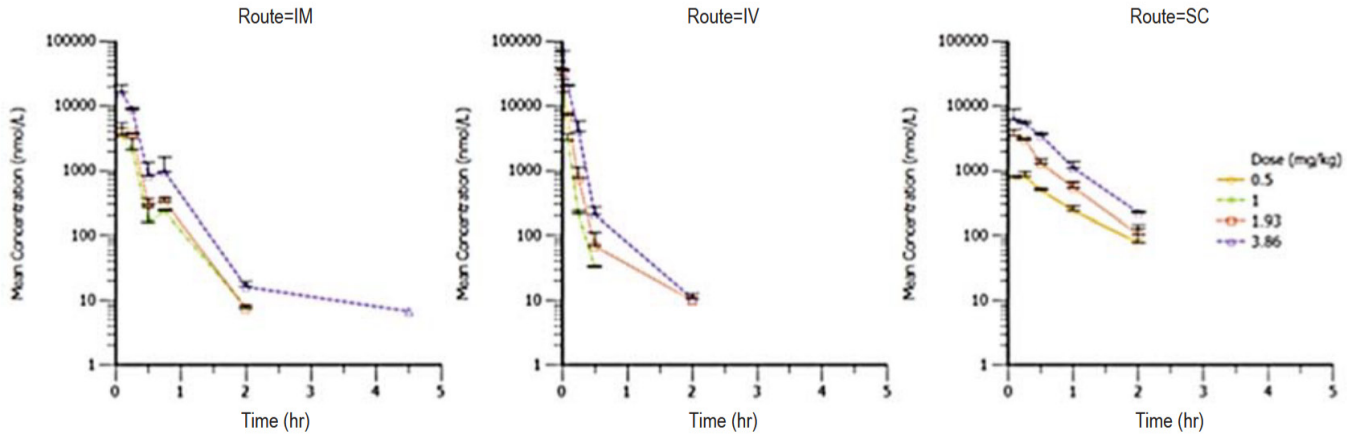
IN-LIFE MONITORING AND SAMPLE COLLECTION

Large animal study designs typically require clinical observations such as body weight observations, food consumption (for NHPs) and behavior changes. Dosed animals are monitored in-life for adverse effects in response to the test article which includes clinical observations and sample collections. Additional in-depth clinical observations are available for therapies that have been reported to cause acute adverse effects. We also offer standard pretreatment regimens to mitigate those anticipated potential transient effects.

In addition to clinical monitoring, Biomere offers several noninvasive sampling at specific timepoints during the study that include biofluid collections (blood, CSF, bone marrow aspirates and urine) as well as tissue biopsies such as skin and liver. Additionally, imaging methods such as fluorescein angiography and electroretinograms (ERGs), optical coherence tomography (OCT) and fundus imaging for ocular studies, IVIS bioluminescent imaging (for specific organs) can be performed to evaluate biodistribution and PK/PD effects.

Once the study is completed, the team performs detailed necropsies that includes tissue and biofluid collections. The team has the expertise to perform CNS microdissections, ocular tissue isolation and dissections etc. Isolated tissues are embedded in OCT, fixed or frozen for downstream analysis.

PK profiles of 4 doses of a novel αIIbβ3 antagonist administered using three different dosing methods (intramuscular, intravenous and subcutaneous) in NHPs.

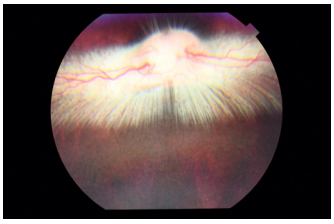


ENDPOINT ANALYSIS:

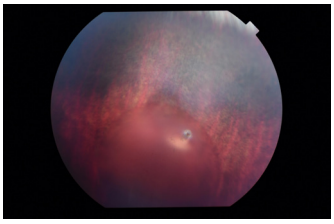
Biomere is actively expanding our portfolio of endpoint assays to include readouts such as mRNA expression (q-PCR), protein expression, coagulation assays, clinical chemistry panels etc. Additionally, we partner with third-party providers for histopathology, mass spectrometry (LC-MS), cell sorting, multi-omics analysis etc. We offer flexible options for down-stream analysis including performing assays in-house, shipping samples to client-specified partners or subcontracting analysis to our partner network. At the end of the study, a complete data package including a data submission or full report are available for delivery.

Fluorescein Angiography of a Normal NHP eye

Color Fundus of a Normal Rabbit Eye



Color Fundus Post-Subretinal Injection in a Rabbit Eye



Fluorescein Angiography of a Normal Rabbit Eye