MANUFACTURING SUPPORT | PROCESS DEV & COMPARABILITY | **ANALYTICAL DEVELOPMENT** | QUANTITATIVE MODELING | QUALITY SYSTEMS | DEVICE DEVELOPMENT

REGULATORY SUPPORT | **PRECLINICAL DEVELOPMENT** | PROJECT & PROGRAM MGMT | MARKET RESEARCH | INTELLECTUAL PROPERTY | FINANCING & DILIGENCE

Analytical Development: Preclinical Evaluation of Candidate Potency Assay

Why DHC?

- EXPAND CLIENT BANDWIDTH
- PROVIDE ADDITIONAL TECHNICAL EXPERTISE
- SOLVE EXISTING PROBLEM (REMEDIATE)

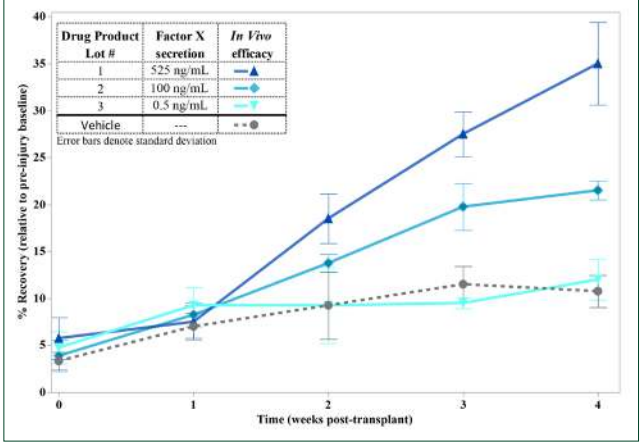
The Ask

Potency assays should reflect efficacy associated *in vitro* and *in vivo* activity. The client requested assistance from DHC with the design and use of preclinical studies to demonstrate biological relevance of their lead candidate *in vitro* potency assay for a clinical stage cell therapy product. This interaction demonstrates a common industry overlap between the service areas of analytical and preclinical development.

DHC's Approach

- The goal of this project was to obtain proof-of-concept *in vivo* data to support the validity of the client's *in vitro* potency assay and to set assay acceptance criteria that could be used to evaluate the lot-to-lot consistency of the client's drug product.
- Dark Horse's extensive experience in preclinical modeling and *in vivo* mechanistic studies provided the necessary know-how to identify a viable strategy for establishing the physiological relevance of the client's *in vitro* potency assay.
- The first step was to evaluate existing preclinical data and identify potential strategies to demonstrate causality between the cell therapy product's activity in the candidate *in vitro* potency assay and the product's *in vivo* therapeutic activity.
- Once an optimal strategy had been selected, DHC provided the client with a detailed design of the proof-of-concept *in vivo* preclinical study, including key outcome measures and a sampling plan that would allow the program to advance beyond correlation and demonstrate a causative role of the product's hypothesized therapeutic mechanism of action.

***In Vivo* Efficacy Plot of Different Drug Product Lots Secreting Candidate Potency Factor X**



The Impact

The outcome of this engagement was the identification of the strategy necessary to verify the physiological relevance of the lead candidate potency assay for a clinical stage cell therapy product.

Next/Concurrent Steps

- Process Development/Comparability Studies
- Preclinical Development
- Regulatory Support
- Manufacturing Support