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

Comparability Review in Preparation for BLA Filing

Why DHC?

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

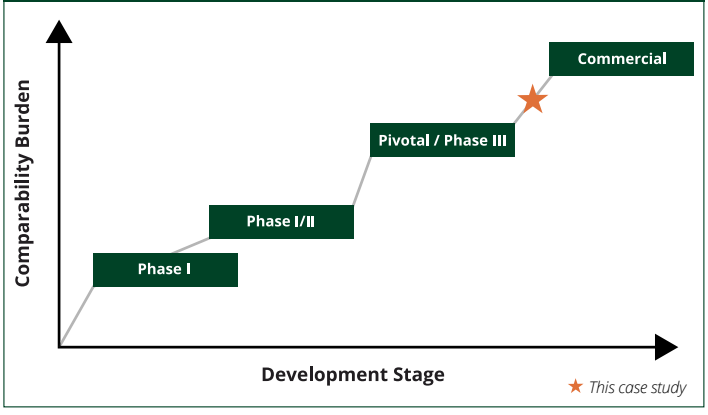
The Ask

The burden of proof of comparability rises sharply by the time therapies arrive at Pivotal/Phase III, especially given the likelihood of manufacturing process changes before arrival at that stage. Add that to the recent string of BLA rejections and late-stage product delays relating to analytical characterization of C&GT products, and any biotech would be wise to proceed with caution. This client, advancing through their cell therapy product's late-stage development review for use in fighting a non-orphan disease, enlisted Dark Horse as a second set of expert eyes. DHC's role was to provide an independent review of their comparability package, complete with a comprehensive gap analysis and risk assessment, in preparation for their upcoming Biologics License Application (BLA filing).

DHC's Approach

- A late-stage project brings with it a significant amount of material (historic data files, documents, agency correspondence, presentations, etc.). The first step was to do an extensive review of the entire history of the Phase I and II clinical trials in addition to a review of prior dialogue with the regulatory agency. This review effectively considered past responses to agency questions or concerns and provided a road map ahead for future expectations and questions.
- In addition to clinical data for safety and efficacy, extensive process data was also necessary for review: manufacturing processes (including changes where relevant) and previous comparability packages.
- Because this project occurred during analysis of the Pivotal/Phase III trial results, additional documents and data continued to come through to the Dark Horse team in real-time as they were generated.
- Dark Horse worked quickly to ensure that the client's internal deadlines remained intact.
- Interim meetings kept the client up to date as the review progressed, providing preliminary feedback and document review questions as well as getting on-the-ground updates as the clinical data analysis continued.
- Once the reviews were complete, the Dark Horse team put together a gap analysis and trademark matrix-based risk assessment of their comparability package and shared those findings with the client along with risk ratings and (where necessary) mitigation recommendations in order to prepare the client to the fullest possible degree for their upcoming interactions with the regulatory agency.

As a therapy proceeds through Phases I / II and into the Pivotal—or Phase III—clinical trials, the comparability burden increases.



The Impact

The comparability package for this client's late-stage cell therapy, which is a therapy with a potentially wide-reaching impact, was thoroughly vetted and ready to be submitted as part of their BLA filing.

Next/Concurrent Steps

Regulatory Support (including authoring or prep/practice for a BLA filing)