



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

# Embedded early for de novo support

## The Ask

Many DHC clients request support when they reach a point in development where they have problems or questions that they cannot answer, or need additional bandwidth to continue. Some clients, such as this pure-play gene therapy client, though, request support very early in the process so as to have continual assistance. In this case, DHC was brought in by the lead investor at company formation, just as its programs were being spun out of academia. Funding was already secured and scalability was a known challenge. Academic data was plentiful but, beyond that, the therapy was in nascent stages. Dark Horse worked with this client from the beginning to conceptualize and build a development process that would stand up to the challenges of each future trial phase and into commercial production.

## DHC's Approach

Besides the need to translate their research achievements into a commercially viable product, the client's manufacturing process would have sufficed for Phase 1...but wasn't scalable (or at an appropriate quality level) beyond that. DHC provided support for all elements of CMC: building a manufacturing process that would prove strong enough to translate into industrialization.

Preclinical proof-of-concept studies by the academic partner included two transgenes and two plasmid systems. DHC consultants re-sequenced the plasmids, transferred to a three-plasmid system to align with current best practices for regulatory compliant AAV production, and led the vendor selection process for plasmid synthesis, cell banking, and production.

After redesigning and manufacturing the plasmids, Dark Horse went through an RFP process to identify a contract manufacturing partner for the vector that would meet the long-term needs of the developer. Particular consideration was given to use of GMP-grade raw materials and a scalable manufacturing platform to limit the degree of comparability testing that would be necessary as development progressed.

Many pieces of the process were happening in parallel, such as working to get sufficient research grade plasmid, while simultaneously beginning the manufacturing of a GMP-grade plasmid to be used later in development.

Regulatory needs were also a consideration in this project. DHC experts wrote the CMC section for the pre-IND and participated in accompanying regulatory discussions.

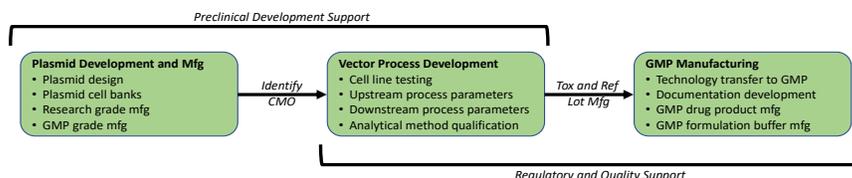
On the process development side, identifying and testing cell lines was top of mind, as was the need for process parameter optimization and demonstration of scalability. The DHC-chosen manufacturer made materials to support preclinical studies at the same time as working through the process development.

Documentation is critical at each stage, particularly when proceeding from development to manufacturing. Dark Horse took point on every GMP document, every batch record, and every analytical qualification, representing the Quality function for the client in review and approval of all manufacturing and test method qualification documents.

Any remediation needs were addressed via technical troubleshooting during development.

## The Impact

Having a DHC team continually engaged as the technical operations lead allowed for support of everything downstream of research: from process development to CMC and regulatory support to manufacturing support, etc. Dark Horse provided certainty that each step was being done to the highest levels of technical proficiency along with the long-range consideration, planning, and analytical awareness that characterize successful therapies. Dark Horse cannot, of course, guarantee the success of any therapy, but our teams *can* guarantee an optimized process and a 360° technical and strategic viewpoint to give therapies the best possible chance at successful commercialization.



## Why DHC?

EXPAND CLIENT BANDWIDTH

PROVIDE ADDITIONAL TECHNICAL EXPERTISE

SOLVE EXISTING PROBLEM (REMEDiate)