Case Study

Ensuring the Path to Compliant Analytical Methods

A Comprehensive CMC Approach to Accelerate Program for Emerging Companies

Service Areas: Cell & Gene Therapy, CMC, Quality
Lifecycle Stage: Clinical, Commercial

A gene therapy company spent over a decade developing their first-generation product, partnering for many early development capabilities. Then when the product was moving into the final stage clinical development, they bought out the rights and now owned 100% of the molecule. However, with a lean organization who had limited CMC and analytical methods experience, they faced challenges in progressing through clinical and CMC development.

Many emerging biotech companies face similar situations. Running ultra-lean and virtual organizations, they require expertise in a range of areas to develop CMC strategies and then manage execution that advances their technologies through clinical and commercial operations. This particular company approached Converge for comprehensive CMC expertise.

From Strategy to Remediation and Execution

Analytical methods development and validation is a critical part of cGMP requirements. It is essential to ensure that methods are robust and can ultimately be validated to enter Phase 3 clinical trials.

Converge experts assessed the status of 12 assays to determine viability for supporting a commercial process. We identified gaps and issues, as well as provided recommendations for methods that needed remediation or replacement. We also developed a strategy for ensuring that the range of methods covers all quality attributes of the product.

Working from that strategy and initial recommendations, our team remediated the gaps and provided oversight for continued methods development. The assay to detect viral contaminants was a particular concern. The treatment utilizes a viral vector to deliver genetic material and achieve the desired therapeutic effect. It is important that the virus only deliver the specified genetic code to the target in order to avoid adverse or off-target effects.

The assay was originally devised early in our client's development cycle to detect viral contaminants. However, with gene therapy and other innovative treatments, cGMP requirements evolve to reflect

current science and understanding. The concern was that the original method would not detect unwanted viral artifacts at the level necessary to meet the current stringent requirements.

Given the client's extensive history using the original method, our team first worked to see if it could be brought up to regulatory standards. We developed a strategy to salvage the original method through extensive testing based on our years of analytical development and Quality Control (QC) experience. Unfortunately, results indicated that the product simply had too high a concentration of non-active virus particles.

In the end, we identified an alternative method because the older method required replacement.

Delivering CMC Expertise Beyond Remediation

In addition to methods development and remediation, the client reaped other benefits along the way. We corrected and revised the acceptance criteria for the potency assays, enabling the company to qualify them and deliver consistent results. Since responsibilities for analytical methods were split between the production site and contract testing labs, our experienced team also provided more routine QC support. This included:

- Training for manufacturing and testing partners,
- Oversight for stability programs extending the product's expiry/shelf life, and
- Managing the change controls for methods transfer to ensure the assays transferred correctly and yielded comparable results.

Status Today

Our client continues to develop their program through clinical studies, while also investing in innovative new gene therapy programs. Our initial work together is serving as a platform for their next generation technologies in areas like establishing bioequivalence. The company can use their previous clinical trial data where applicable to proceed into Phase 3 with new molecules.

As they progress, the client is also building out their internal organization and capabilities. Our team continues as a partner by:

- Filling gaps in expertise,
- Accommodating spikes in the level of activity,
- Bringing in new capabilities before the client is ready to hire, and
- Providing guidance from a legacy point-of-view in support of their full product portfolio.

Ultimately, this innovative gene therapy work brings our client closer to a point where their life-saving treatments will reach patients around the world.

Converge Consulting *serves the Life Sciences industry with strategy, operations and execution expertise. We collaborate with biotech, pharmaceutical and cell/gene therapy companies to achieve important business objectives. The Converge approach focuses on bridging the gap between sound strategy and reliable execution. www.convergeconsulting.com*