

# Advanced Analytical Approaches for Improved Development of Cell and Gene Therapies



## Introduction

Cell and gene therapies have the potential to provide long-term therapeutic efficacy, but their development is both risky and cost-intensive. Obtaining a better understanding of the specific structural attributes of vector proteins that influence clinical delivery and outcomes is essential for advancing both individual candidates and the platforms on which they are based.

Strategic application of advanced analytical techniques can help improve selection of candidates and guide development decisions, leading to a greater number of safer, more efficacious cell and gene therapies successfully completing development and entering the market. High-resolution LC-MS based characterization, quantification and *in vivo* expression profiling approaches are increasingly being applied to enable improved program understanding, controls and clinical outcomes assessment.

## Highlights

We apply advanced analytical approaches for enhanced development of cell and gene therapies including:

- ✓ Vector Protein Characterization and PTM Analysis; Correlations to Infectivity
- ✓ LC-MS HCP Profiling in Vector Production Lots
- ✓ Identification and Quantification of Gene-Edited Proteins in Target Cells and Tissues
- ✓ Quantitation and Characterization of Expression Products in Cells, Pre-Clinical and Clinical Samples

## Applications of Mass Spectrometry in Cell and Gene Therapy Product Development

LC-MS and intact MS can be used to analyze the detailed sequences of the vector proteins, as they confirm identity through complete amino acid sequence coverage, enabling analysis of sequence variants, PTMs, and splice variants. Peptide mapping by LC-MS coupled with intact protein analysis can be used to characterize the N-termini of VPs, establish VP ratios, and differentiate AAV serotypes using accurate mass measurement. Detailed LC-MS-based characterization can be used to identify and quantify key PTMs, and more importantly, is accelerating product development. These tools have increasingly become expected standards in the development of cell and gene therapy products as they may impact the potency and stability of the product.