MilliporeSigma

viral vector Manufacturing

Capabilities and Experience

BioReliance®

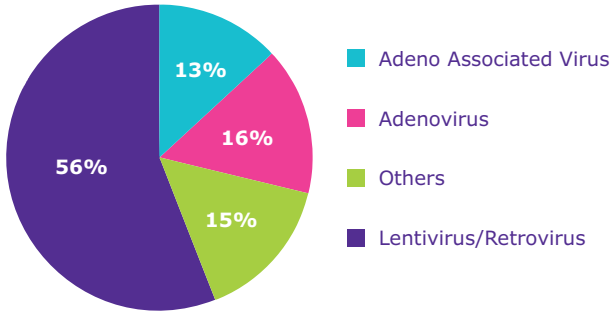
Pharma & Biopharma
Manufacturing &
Testing Services

Viral & Gene Therapy Manufacturing

Why we are the best strategic partner for you:

- **More than 25 years' experience** manufacturing viral vectors for pre-clinical studies to commercialization
- **Highly qualified experts** invested in the process development, scale-up, tech transfer, and manufacturing of viral vectors
- Process Development/Tech Transfer/ Manufacturing teams with **proven history of successful tech transfer and continuous Process Improvement**

Historical Experience by Virus Type
(>550 batches from 2010–Present)



- Proven scalable platforms to **overcome production challenges** with Lentivirus and Adeno-Associated Virus (AAV)
- Project Management team is dedicated to **keeping both manufacturing and development projects on time**
- Our Product Development Process (PDP) **ensures development of a risk-based and scalable processes** designed to build **solid foundation for commercialization**
- **Established synergy between production and testing within one company** supporting early development through commercial production
- **Proven FDA/EMA compliant** Quality Systems for commercial release of approved products
- History of successfully **navigating the commercial regulatory pathways**

Quality Assurance and Regulatory Expertise:

- Inspected by the United States Food and Drug Administration (FDA)
- Inspected by the European Medicines Agency (EMA)
- Remote (Paper) Inspections
  - Pharmaceuticals and Medical Devices Agency (PMDA) Japan
  - Therapeutic Goods Administration (TGA) Australia
  - Health Canada
- Licensed by the California Department of Health Services, Food and Drug Branch (FDB)
- Inspected by the Services Food and Drug Branch (FDB)
- Site Master File covering our Facilities and Quality Systems has been referenced by over 100 Client Submissions
- Audited regularly by USDA, San Diego County, and Clients with ex-FDA inspectors and European QPs

Who We Are

Virus and Gene Therapy Solutions

Carlsbad, California, USA

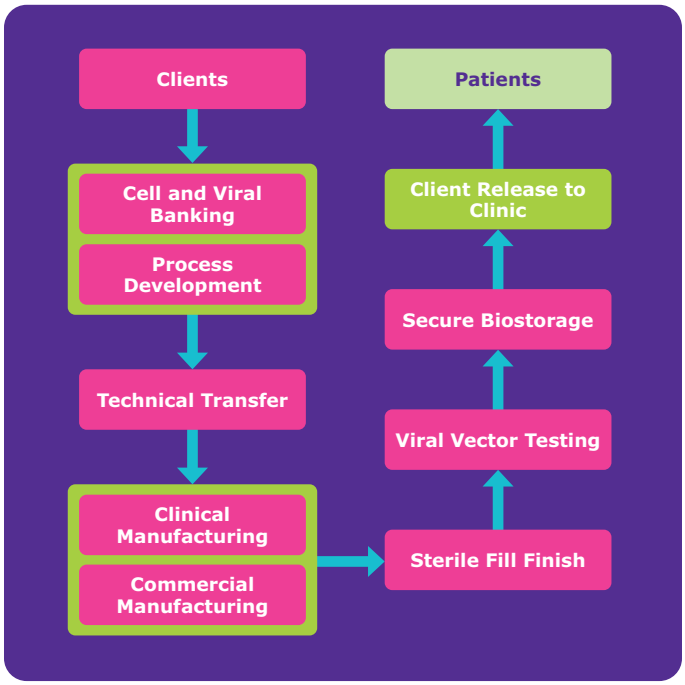
- GMP Virus Production
- In-process testing
- Process Development Services

Small Scale Facility

- 65K ft²/16 suites/ 2 manufacturing buildings
- Small scale clinical and commercial
- Adherent, suspension up to 200 L

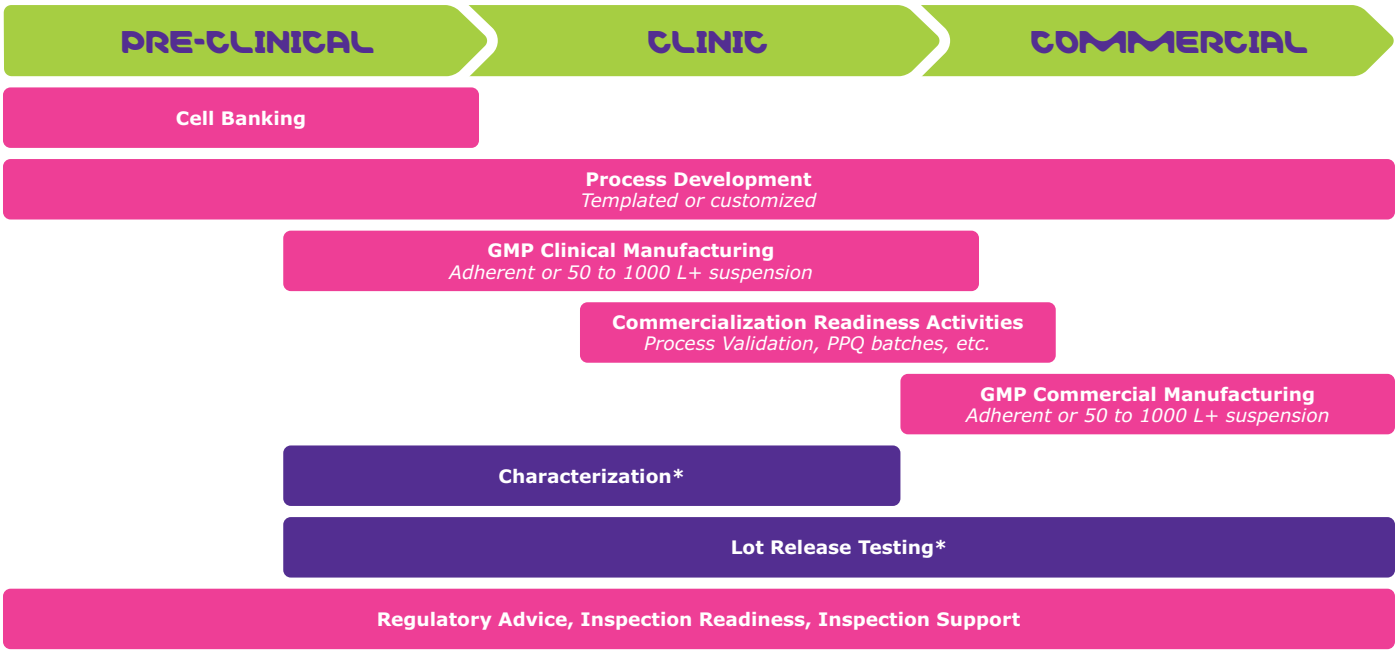
Large Scale Facility

- 92k ft²/11 suites
- Large scale clinical and commercial, +1000 L scale
- Quality control



Process Overview

Development, manufacturing, and testing in one contract



**BioReliance® testing services are conducted at our facilities in Glasgow, UK and Rockville, Maryland, USA.*

what we bring to the table

Industrial-scale GMP Viral Vector Manufacturing

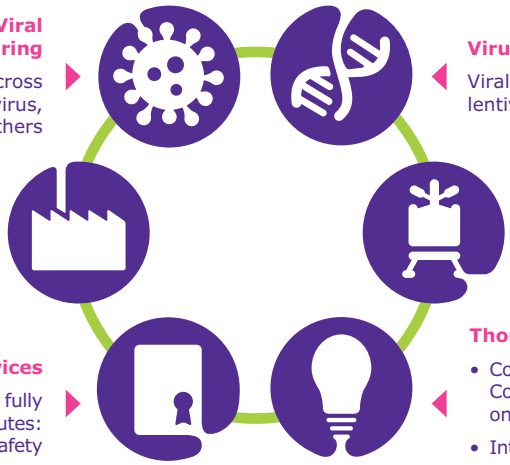
Deep experience and know-how across virus types, including Lentivirus, Retrovirus, AAV, and others

GMP Manufacturing Services

Cell line development, biological production, commercial manufacturing

Industry-Leading Testing Services

Biosafety and characterization to fully analyze a vector's critical quality attributes: purity, identity, potency, and safety



VirusExpress® Production Platform

Viral vector platform process for lentivirus and AAV

Best-in-class Bioprocessing Reagents and Equipment

Including upstream and downstream processing

Thought Leadership

- Core member of National Cell Manufacturing Consortium and developed national roadmap on cell therapy manufacturing
- Internal Bioethics Advisory Panel established on gene editing

Manufacturing overview

Cells & Virus Experience	
Cells	293, 293T, BHK, PER.C6, MRC5, HeLa, HT1080, A549, and Vero
Viruses	AAV, Adenovirus, Lentivirus/Retrovirus, Reovirus, Dengue Virus, Herpes Simplex Virus, Coxsackie Virus, and others

Viral Production Scales	
Adherent	Up to 40x10 layer CellSTACKS®, 20xHS36 layer HyperSTACKS®, iCELLis® 500
Suspension	50 L, 100 L, 200 L, 500 L SUB, 1,000 L SUB, 100 L/1,000 L perfusion

Fills	
Fill/finish	**Semi-automated**: 800 vials/day in 2 mL to 30 mL vials **Automated**: 2,000 vials/day in 2 mL to 30 mL vials

Process Development Services

Our team possesses significant R&D and process development capabilities including "end-to-end" processing over multiple scales, modalities, and viral vector types.

Process Development Standard Equipment:

- Ambr® Cell Culture High Throughput Bioreactor
- Mobius® Single-use Bioreactor from the Millipore® portfolio
- iCellis Nano Fixed Bed Bioreactor
- Eppendorf CelligenBlu Bioreactor
- Eppendorf DASGIP
- AKTA Prime
- AKTA Pilot
- Spectrum TFF System
- PendoTech Filtration System

Process Development Adherent Scale Equipment:

- 10 x CS10
- 20 x HS36
- iCELLis Nano (up to 4 m^2)
- Access to iCELLis 500 m^2

Process Development Suspension Scale Equipment:

- 3 L, 50 L, and 200 L Mobius® Single-use Bioreactors from the Millipore® portfolio
- 50 L Hyclone Single-use Bioreactor
- Up to 50 L Eppendorf CelligenBlu Bioreactor

Upstream

- Optimization of (planar) adherent cell culture processes
- Development of SUB processes (in microcarrier mode or single cell suspension)
- Transfection optimization
- Development of scaled up cell culture processes

Midstream & Downstream

- Virus clarification
- Chromatography development and optimization
- TFF development and scale up
- Ultracentrifugation

Analytical Methods

- P24 and AAV ELISAs
- qPCR; ddPCR
- Bioassays with imaging (cell based)

VIAL THAW

DRUG SUBSTANCE

Release your therapy with confidence

As gene therapy products continue to deliver remarkable results, biosafety testing and characterization remain a critical part of the development process. These vital steps help mitigate safety concerns and provide a better understanding of products and processes well in advance of patient administration. With our comprehensive biosafety testing and product characterization portfolio, custom analytical method development capability, and technical expertise, we partner to develop a testing strategy to fully analyze the critical quality attributes of your therapy. Our BioReliance® services give you the confidence to advance your therapy to market quickly and safely.

Viral vector development and production services

For gene and cell therapies, we work closely with our global teams in Rockville, MD, Glasgow, UK, and Singapore to develop and support testing services specific to that specialized area. Our facilities in the U.S., Europe, and Asia have a trusted and collaborative relationship with regulatory agencies around the world, including FDA, EMEA, and MHRA.

about us

Established in Darmstadt, Germany in 1668 by Friedrich Jacob Merck, we are the world's oldest pharmaceutical and chemical company.

Over the course of the past 350 years, we have built a truly global company. Our >58,000 employees span 66 countries and are united by their passion for new ideas, the possibilities of technology, and the potential to make a difference in the world.

To place an order or receive technical assistance, connect with us at

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