Viral vector CDMO services

Decades of unmatched viral vector expertise, from concept to delivery

Viral vector services (VVS)

Experience, capacity, and breadth of technical expertise and capabilities.

With over 20 years of experience manufacturing a broad range of viral vector products, VVS is well-equipped to handle your unique product needs. Our network of sites contains 400,000+ square feet of manufacturing space with more than 40 suites and capacity to expand. In addition, our breadth of integrated services ensure smooth transitions and expertise across your value chain.

Experience

- 20+ years of cGMP experience
- 200+ viral vector products manufactured over time
- 900+ viral vector GMP lots manufactured over time
- 3 commercially approved products and several others pending

Capacity

- More than 400,000 square feet
- 38 drug substance suites
- 6 drug product suites
- 3 late-phase/commercial manufacturing facilities
- Experience with 12+ AAV serotypes
- 10 manufacturing modalities

Capabilities

- Full-service viral vector CDMO
- Experience with 12+ AAV serotypes
- 10 manufacturing modalities
- Leverage Thermo Fisher's technology, cell lines, equipment, products, and logistics
- Access to a breadth of integrated services

While the viral vector market is dominated by adeno-associated viruses (AAV) and lentiviral vectors (LV), there is also a range of less commonly used vectors. If you have a novel system, we're excited to learn about it. Regardless of your vector strategy, you can be confident that we have the experience and resources to smoothly manage any project.

Table 1. Support for a variety of vector manufacturing strategies

Vector type	Manufacturing modality*	
AAV	Adherent + suspension	Suspension + HSV
	Producer cell line + adherent	Suspension + baculovirus
Adenoviral	Adherent + suspension	
Herpesviral	Adherent + suspension	
Lentiviral	Packaging/producer cell line	
Retroviral	Packaging/producer cell line	Adherent + suspension
Key	Mammalian cells; Mammalian cells transient transfection; Mammalian cells infection; Insect cells	

* Additional manufacturing modalities also available; inquire for more information

Viral vector capabilities overview

Broad capabilities, flexible equipment options, and robust analytics.

From process development and process characterization to manufacturing, QC, and fill-finish, VVS has the broad capabilities and expertise needed to develop and manufacture your viral vector product.

Table 2. Process development and characterization capabilities

Upstream processing	Downstream processing	Assay development and analytics	Process sciences
• Molecular and viral cloning • Seed train and vector production via transfection, viral infection, and stable production – Cell lines (mammalian, insect, PCL, adherent, or suspension) – Technologies (flatstock, iCELLis, SUB, perfusion) • Full process customization and development (Ambr®, DOE, iCELLis Nano, scale-up)	• Purification of common and novel vector types • Chromatography-based • Optimization as needed – Increase yield/recovery – Full capsid separation – Specific purity requirements • Broad range of purification technologies	• Assay establishment, customization, or development • Platform assays for various vector types • Process development testing support • Preclinical material testing • High-throughput analysis for rapid support	• Analytical support • Process establishment and engineering • Process characterization – Risk assessments, CQAs, product profile – Scale-down model qualification – Satellite campaign batches

Table 3. Manufacturing capabilities

MS&T and process validation	Manufacturing	QC	Fill-finish
• Manufacturing support studies • Process validation plan and strategy • FMEA • Validation support studies • PPQ	• Suspension and adherent modalities • Clinical- and commercial-scale capacity • Broad range of technologies and equipment • Cell and viral banking	• Compendial assay verification, assay qualification, and validation • DS and DP in-process and batch release testing • cGMP stability studies • Reference standard qualification • Assay bridging and product comparability studies	• Formulation evaluation • Semiautomated and automated fill lines (Bausch+Ströbel, Optima) • Prequalified vial configurations • Primary vial labeling and packaging • Up to 5,000 vial fill capacity per lot

Flexible equipment options

Supporting your unique process needs.

Sites are equipped with flexible options to scale adherent or suspension manufacturing processes, upstream and downstream processing, and fill-finish. In addition, suites can be configured to meet additional process requirements, ensuring maximum flexibility to accommodate your unique needs.

Table 4. Technology options across phases and sites

	PD/Phases 1 and 2	Late-phase/commercial		
Platform	**Gosselies, Belgium**	**Cambridge, MA**	**Plainville, MA**	**Seneffe, Belgium**
Adherent	24CS10 and 15HS36	iCELLis 500, 40CS10, or 48HS36	Flex	24CS10 and 15HS36
Suspension HEK293	Up to 2 x 200 L	2 x 200 L	Up to 4 x 200 L Up to 2 x 2,000 L	Up to 2 x 200 L
Suspension Sf9/baculovirus		Up to 2,000 L		Up to 2 x 1,000 L
Suspension other		Up to 2 x 200 L Up to 2,000 L		Up to 2 x 200L Up to 2 x 1,000L
Fill-finish equipment	N/A	Bausch+Ströbel KSF5105 Up to 500 vials (10 mL) Up to 2,500 vials (2 mL)	Optima VFVM 7000 Up to 5,000 vials	Bausch+Ströbel KSF5105 Up to 10,000 vials
Alternative scales, technologies, and platforms (i.e., perfusion-based systems) available.				

Analytical development and testing

Supporting a robust manufacturing process.

Analytical development and testing is critical to ensuring the development of robust processes and products that meet regulatory requirements. By using in-house resources and methods and continually investing in new technologies, we have created an agile response to adhere to changing regulatory and customer requirements. Consistent method execution ensures streamlined batch release testing, further accelerating the release of your product.

Table 5. Viral vector analytical testing services

Critical quality attributes	Assay and testing methods	
Strength/potency	• Vg titer • Infectious titer • Transduction assays	• Capsid titer • Potency assays • Infectivity
Impurities/purity	• Residual DNA (host, plasmid, helper) • Residual HCP	• Aggregation • E:F caspid (AUC)
Safety	• Adventitious agents • Sterility/bioburden • Mycoplasma	• Endotoxin • rcAAV/rcL/rcA
Other assays/particles	• Particle concentration (HPLC) • Capsid ELISA • Total protein/DNA	• Genome integrity • A260/280

Global viral vector services network

Four global locations, ONE connected team.

Technical comparability

- Identical or comparable equipment assets for the same process and scale-down practice
- Standard platform process solutions for early-phase projects
- Standard tech transfer process

Talent competence

- Centralized Bioprocess Sciences leadership management
- Standard talent strategy to recruit and retain team members
- Regular communication between sites for knowledge and experience exchange

Capabilities	USA	EU
Process development	✓	✓
Analytical development	✓	✓
Process characterization	✓	✓
Clinical- and commercial-scale GMP manufacturing	200 - 2,000 L	200-1,000 L
QC in-process, stability, and release testing	✓	✓
Drug product fill-finish	✓	✓

Tech transfer and process development

Phased approaches and collaborative readiness assessments ensure smooth transitions.

Technology transfer from a sponsor company to its CDMO of choice can be one of the most critical stages of development. A full understanding of available data and product requirements is necessary to ensure comprehensive gap and risk assessments and the development of product-appropriate batch records, SOPs, and product specifications. A phased approach can help ensure a smooth tech transfer process—and subsequent process performance qualification activities—so that cGMP manufacturing can start as soon as possible.

Table 6. Phased approaches to (A) technology transfer and (B) process performance qualification

A.

Information transfer	Information assessment	Execution
• Project schedule • Team roles • Available data transfer • Initial facility fit • Raw materials assessment	• Detailed gap and risk assessment • Bill of materials • Detailed process descriptions • Sample plan • Process development/characterization/ pilot runs (if needed)	• Batch records • SOPs • Spec development • ENG and GMP run execution

B.

Phase 1	Phase 2	Phase 3	Phase 4
Process definition • Process characterization/ process understanding • Shipping studies	**Process validation** • PVMP • PPQ runs • Support PQs – Buffer/media hold studies – Clean hold time studies – Buffer/media mixing studies	**Continued process verification (short-term)** • Controlled by CPV plan • Generation of intermediate process control limits • Finalization of process control limits	**Continued process verification (long-term)** • Controlled by trending program • Process monitoring for control • Evaluation for process health

Regulatory services

Delivering cell and gene therapy regulatory expertise across the product life cycle.

The advanced therapies regulatory landscape is continually evolving, and what is acceptable today may not be acceptable tomorrow. With over 15 years of experience supporting customers with global regulatory interactions (USA, EU, and Canada), CMC regulations, guidelines, and inspections, we have developed an approach that is well-suited to evolving requirements. Working in concert with our process development and manufacturing technical experts, our regulatory services team can help reduce the number of intermediaries and filing lead times by providing document review, gap analyses, and document preparation to support your regulatory filings.

Regulatory dossier preparation

- **Author and/or review CMC dossiers (complete or partial modules) for major jurisdictions in CTD format:**
  - Early- and late-stage development
  - Marketing applications
  - Post-approval changes
- **Regulatory submissions strategy**
- **Responses to health authority questions**

Regulatory meetings support

- **Assistance in regulatory agencies pre-submission/advice meetings:**
  - Filing strategy outlines
  - Requests
  - Briefing books
  - Minutes

Regulatory expertise provision

- **Strategic regulatory consulting**
  - Regulatory review and gap assessments
  - Ad hoc advice across product life cycle
- **Project regulatory liaison**
- **CMC-specific trainings and workshops**

Regulatory compliance support

- **Site foreign registration packages**
- **Site-related reference documents**
- **Product-related documents (e.g. declarations)**
- **Change controls evaluation**
- **Document legalization**

Viral vector service offerings

Different pathways to address your unique program needs.

To provide flexibility and agility for our customers, we offer several different pathways for viral vector development to support various manufacturing strategies, timelines, and customization needs. This includes standardized processes for AAV and LV, as well as fully customized approaches for a variety of vector types.

	Rapid Development Framework™ (RDF)	Customizable development program	Client tech transfer program
Viral vector type	AAV and LV	AAV, LV *Others (AdV, RV, HSV, MVA, VSV, etc.)	AAV, LV, AdV, RV, HSV, MVA, VSV, etc.
Vector manufacturing	HEK293 transfection	HEK293 transfection, Sf9 baculovirus infection, *others	Tech transfer and validation of customer process
	Suspension and chromatography-based purification	Suspension (up to 2,000 L) and *adherence (includes fixed-bed bioreactor)	Scale up from pilot to commercial manufacturing
	Process feasibility	High-throughput screening for viral production and purification steps	Varying upstream/downstream unit operations and technologies
Analytics	Standardized assays	Extended characterization assays and *customized development	Assay transfer or development
Time to GMP drug product	9 months	AAV/LV high-throughput: 9 months *Full development and others: 12+ months	9+ months
Value	Reduced program cost and accelerated path to GMP leveraging tested process and analytics	Accelerated high-throughput development for improved process characterization, productivity, and quality	Direct transfer and manufacturing

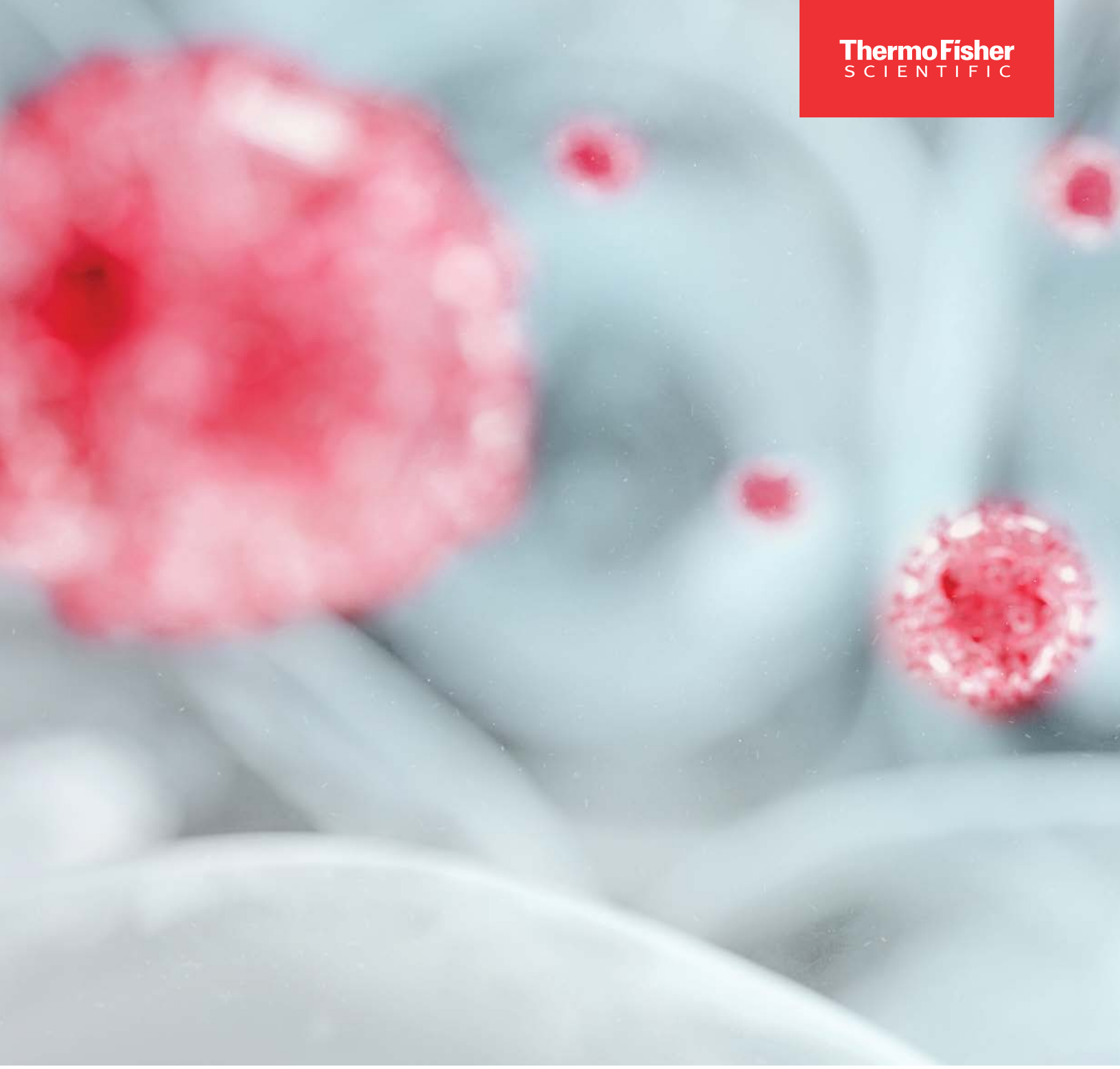
*Applies to other vector types outside of AAV and LV

Integrated services for advanced therapies

De-risk your program and get to market faster.

Integrated services can reduce risk in both development and manufacturing by streamlining handoffs and allowing key processes to run in parallel. One key risk area that is often overlooked is the early establishment of manufacturing controls when transitioning from early discovery work to clinical manufacturing. That's why we offer early translational services to help streamline your translational research and rapidly identify lead therapeutic drug candidates. Translational services utilize established, scalable processes with the advanced analytical testing that is characteristic of future cGMP workflows to support candidate drug selection.

Translational services	Viral vector development and manufacturing	Cell therapy development and manufacturing	mRNA development and manufacturing	Clinical supply services
• Scaled-down processes, qualifiable assays, high-quality materials • Viral vectors • Cell therapy • Molecular biology • Analytics	• Adherent and suspension modalities • Small- to large-scale manufacturing • AAV, LV, AdV, RV, MVA, VSV, and other viral vectors • Virus-like particles	• Autologous and allogeneic • Viral and non-viral modified gene delivery systems • T-cells, NK cells, iPSCs, MSCs, APCs, hESCs, and more	• Linearization • mRNA synthesis • Post-IVT modification • Encapsulation • Sterile fill-finish	• Specimen cold chain logistics and cryogenic storage • Clinical and commercial packaging, labeling, and distribution • Qualified shipping solutions and specialty courier services collection, cold chain logistics, and cryogenic storage • Qualified shipping solutions and specialty courier services



Learn more at **thermofisher.com/patheon**
or email us at **pharmaservices@thermofisher.com**
or call **+1 919 226 3200**