ThermoFisher SCIENTIFIC

LARGE MOLECULE DEVELOPMENT AND MANUFACTURING

COMPREHENSIVE OFFERING ENABLING SPEED AND FLEXIBILITY

- API
- BIOLOGICS
- VIRAL VECTOR SERVICES
- EARLY & LATE PHASE DEVELOPMENT
- CLINICAL TRIAL SOLUTIONS
- LOGISTICS SERVICES
- COMMERCIAL MANUFACTURING

patheon

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HOW A SMALL STARTUP WAS ABLE TO SCALE UP, WITHOUT LOSING THEIR PRECIOUS MATERIAL.

Jeff faced a dilemma: how to complete a large biomanufacturing scale up with the very small amount of material his client gave him. And the stakes were high. His client had spent a lot of time and money developing this potentially revolutionary Alzheimer's treatment. Any wasted material would put the execution of the clinical trial at risk, and possibly risk the future of the entire program. Jeff knew the process needed to be perfect. So, his team worked tirelessly to find ways to improve the cell culture performance. They examined key process parameters and even completed additional work in the process development laboratory to ensure success. The result was a flawless scale up and, most importantly, a potentially breakthrough drug was able to get into the clinic.

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Start here, stay here

Supporting you all the way, from discovery to commercialization

Your large molecule has the potential to shape the future of patient care, and when patients are waiting for life-changing medications, meeting the strict timelines of your drug development process is critical. The demand for advanced therapies continues to increase, so you need a partner you can trust to help bring your drug to market reliably, efficiently, and on time.

Thermo Fisher Pharma Services is a full-service CDMO that has the expertise and comprehensive capabilities to seamlessly manage every step of your drug development and manufacturing journey—streamlining your process so you can get to market quickly. As a collaborative partner, we have a shared goal of helping you succeed. We have the skills and experience to help you mitigate risk and respond with flexibility, from drug substance to drug product to clinical trials, and all the way to commercial manufacturing.

Our capabilities

POSITIONING YOUR LARGE MOLECULE FOR EARLY SUCCESS WITH OUR INTEGRATED SOLUTIONS

Our integrated end-to-end solutions are flexible and completely customizable to your large molecule. By partnering with a single vendor, you can remove complexity and bring your large molecule to market quickly, with less cost and reduced risk.

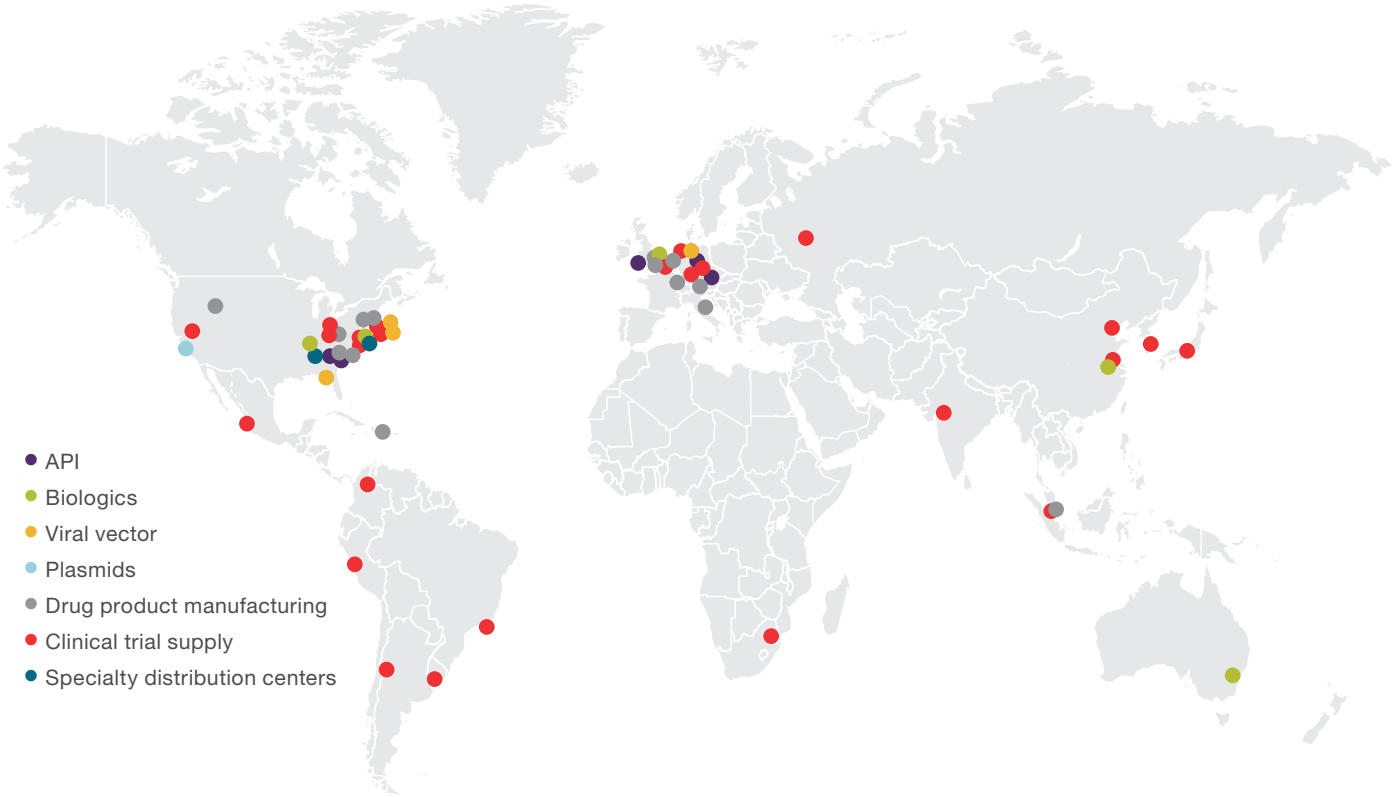
We leverage a broad range of technologies and clinical services to provide robust, tailored solutions that help accelerate, simplify, and improve drug development and manufacturing. Collaborating across drug substance, drug product, clinical manufacturing, and clinical supply, our global team of experts will work with you to quicky overcome any challenge—from complex chemistry to scaling up manufacturing.

Simplify complexity across your regional and global strategy

We have an expansive global network of over 65 sites across five continents comprising technical, quality, and customer engagement teams to support your drug development journey.

Our scientists and engineers apply a science-driven, risk-based approach to the development and manufacturing process, focusing precisely on every step, but never forgetting the end goal of navigating your large molecule toward commercial success.

Thermo Fisher supported 650+ new large molecule projects from 2018-2020



Biologic drug substance

LARGE MOLECULE DRUG SUBSTANCE SOLUTIONS

Solutions to support the full lifecycle of your large molecule biologics

From preclinical to commercial production, our global network of experts understand the long and complex development journey and are committed to help speed your large molecule through early-phase trials and prepare you for commercial success.

We apply our deep process development skills to significantly increase the batch yield and reduce processing time for your molecule. Our proven track record of scaling up biologics helps provide you with cost and time savings at every stage of development. Our unmatched experience working with new large molecule projects allows us to expertly handle any challenges your molecule can present.

Early-stage clinical supply

Early-stage clinical supply of biologic drug substance is produced at state-of-the-art cGMP facilities in Europe, North America, and Asia. A team of experts will surround your discovery with a full range of technologies and analytical services to not only run the project with the highest flexibility, but also deliver on time with exceptional yields and superior quality.

Complete upstream and downstream processing solutions

Our comprehensive upstream and downstream process development capabilities and commitment to innovation, quality, and service make us the ideal partner for the process development of your large molecule projects. Our experts have the skills and experience to develop an optimal process with long-term commercial manufacturing in sight, including:

- Cell line development
- Broad mammalian cell culture experience: mAbs, fusion proteins, bi-specifics, enzymes, fragments, and other recombinant proteins
- Fed-batch, perfusion, and XD® cell culture processes
- Design of Experiment (DoE) studies
- Sartorius Ambr® 15 and 250 microbioreactor systems
- Glass and single-use bioreactors (3 L to 250 L)
- Media/feed strategy optimization
- Resin screening
- Tecan Freedom EVO® platform with Repligen RoboColumn® system
- UF/DF development
- Virus clearance studies
- Process and product characterization

Once preclinical development is complete, our award-winning tech transfer team will move your project to a cGMP facility for scale-up and production. We then develop stable and repeatable processes ready for validation by the FDA.

Commercial manufacturing

We offer commercial biologic manufacturing under full cGMP conditions with speed, efficiency, and exceptional quality, plus the flexibility to adapt to changes in your journey and the market. You will have access to end-to-end, fully integrated solutions for both drug substances and drug products, delivered on time and on budget. As part of the establishment of your commercial supply of biologic drug substance, we provide a complete validation package according to regulatory and cGMP guidelines, including:

- Process validation with critical parameters
- Validation of analytical assays
- Release testing
- ICH stability testing
- Container shipment studies
- CMC documentation in CTD format

"Great skill and leadership in manufacturing, program management, [and] analytical stability." —Biopharmaceutical company focused on autoimmune diseases, USA

Quick to Clinic™

SHORTENING TIMELINES TO IND WITHOUT COMPROMISING QUALITY

We understand the challenges and the need for flexibility and speed in meeting important milestones on your journey to IND. Our Quick to Clinic solution is an innovative platform developed to help shorten the time from transfection to IND to as little as 13 months. The Quick to Clinic solution combines drug substance and drug product development, clinical manufacturing, forecasting, demand planning, and clinical trial supply execution capabilities into a single solution to accelerate your discovery to proof of concept.

Now you can meet important milestones such as filing your IND and securing additional funding with confidence.

Reach milestones quickly

Shorten your early development phase to as little as 13 months from the start of transfection to IND with best-in-class technologies, allowing you to file more quickly and secure funding.

- Cell line development
- Cell culture and purification processes
- Liquid-filled vial drug product formulation

Manage risk

Speed doesn't mean opening yourself up to risk. Using a tried-and-tested process platform from a company with deep experience means you don't have to sacrifice quality for speed.

- Analytical methods
- Early non-GMP material for toxicology studies

Prepare for long-term success

Focus on today's challenges and let us prepare you for the future. Getting your molecule from post-discovery to IND quickly is just the first step. A royalty-free licensing option, high-yield expression system, and robust process platform prepare you for long-term commercial success.

- Released GMP drug substance
- Released GMP drug product
- Viral clearance and stability study data

What you provide	What we use	What we do	What you get
Starting material: Gene • DNA sequence–genetic code	• Thermo Fisher Scientific Gibco™ Freedom™ ExpiCHO-S™ Platform • Patheon pharma services' platform process and Thermo Fisher media/feeds with commercially available raw materials	• Cell line development using Berkeley Lights Beacon® System • Evaluation of upstream and downstream platform processes using high-throughput automation technologies such as Ambr® 15 microbioreactor and Tecan miniaturized purification platform • Formulation screening • Analytical method establishment and qualification • Toxicology batch • cGMP batch: 500–2000 L • Viral clearance study • Stability testing	• Early toxicology material • Released drug substance • Released drug product • Minimum one-month stability data for IND • Templated quality-review reports • Clinical trial packaging and labeling (optional) • Regulatory CMC dossier for IND/IMPD filing

"Exceptional speed and responsiveness." —Biotechnology company focused on oncology, USA

Sterile drug product

DEVELOPMENT AND COMMERCIAL MANUFACTURING CAPABILITIES OF DRUG PRODUCT

Comprehensive development and clinical manufacturing

By working with a single partner for both your drug substance and drug product needs, you are improving decision-making and optimizing outcomes to ensure the success of your molecule. And with the rapid 10% growth of sterile drug products over the past five years, we understand the critical need for fast, flexible solutions and customized processes to keep you on track for commercialization.

We have extensive sterile injectable product development and manufacturing capabilities at all scales. We offer experience, reliability, and a broad range of sterile fill/finish commercial capabilities for liquid-filled and lyophilized vials, including world-class expertise in lyophilization and for pre-filled syringes and cartridges. We have an unrivaled record of sterile drug product commercialization success for our customers, and more than one-third of our commercial manufacturing product launches originate from our formulation and development programs. Leveraging our commercial production and clinical trial solutions will give you extensive access to global technical experts, scale, capability, global regulatory insights, and transportation.

Throughout the entire process of developing and manufacturing your drug product, we will work closely with you to:

- Overcome complex formulation challenges such as solubility and stability
- Build a robust process development program
- Navigate a complex regulatory environment (IND, filing, etc.)
- Provide analytical solutions and data generation for successful regulatory submissions
- Build a business continuity strategy
- Shorten timelines to get to market more quickly

Scale-up capabilities

We provide both clinical- and commercial-scale capabilities at our facilities. Our team has more than 30 years of experience developing, optimizing, and scaling up bioprocesses for clinical and commercial cGMP manufacturing. With 15 commercial lines, nearly 2,000 m^2 of lyophilization capacity, and full formulation and process development capabilities at all sites, scaling up is fast and seamless.

Thermo Fisher was the leader in sterile outsourcing from 2011-2020; manufactured more sterile dose NMEs than the next two highest CDMOs

Produced 132 million sterile and lyophilized vials in 2019

FORMULATION DEVELOPMENT

Get your formulation right the first time

Ensuring that you have the correct formulation from the start of early development can help save time and money as you advance through each phase and on to commercialization. We offer specialized expertise in formulation development, lyophilization, cycle development, process development, and commercial scale-up. Our experts in early development formulation can help you overcome complex formulation challenges to advance drugs to clinical trial with speed and agility.

Gain access to an integrated drug formulation program that is tailored to your large molecule to help you overcome common formulation challenges including:

- Small and large molecules—whether it is a liquid or lyophilized formulation
- Lyophilization cycle optimization
- Temperature and shear-sensitive compounds
- Poorly soluble compounds
- Stability challenges
- Highly potent compounds
- Container closure system selection

DOSAGE FORMS

Broad range of dosage forms to meet your molecule's unique needs

We are dedicated to ensuring that your discoveries have the right dosage forms. Our global facilities manufacture more than 100 dosage forms and provide complete fill and finish services for parenteral drug manufacturing, including liquid and lyophilized products in vials, prefilled syringes, and cartridges.

Sterile dosage forms, commercial and development

	GREENVILLE, NC, USA	FERENTINO, ITALY	MONZA, ITALY	GREENVILLE, NC, USA	FERENTINO, ITALY	MONZA, ITALY
	Development			Commercial		
Liquid vials	2–20 mL	2–100 mL	2–100 mL	2–65 mL	2–500 mL	2–100 mL
Lyophilized vials	2–20 mL	2–20 mL	2–100 mL	2–65 mL	2–25 mL	2–100 mL
PFS/Cartridges	0.5–20 mL		0.5–20 mL	0.5–20 mL		0.5–20 mL

1. ISO and non-ISO vials can be accommodated.
2. Additional vial sizes are available and can be shared by a Thermo Fisher representative.
3. Development scale manufacturing capabilities are suitable for clinical trial material manufacturing.
4. Disposable (single-use system) manufacturing options are available.
5. New capabilities are continually being added. A detailed list of current capabilities can be made available on request.

A world of dosage forms

		STERILE DOSAGE FORMS			
		Liquid-filled vials	Lyophilized vials	Prefilled syringes	Prefilled cartridges
NORTH AMERICA	Bend, OR, USA				
	Cincinnati, OH, USA				
	High Point, NC, USA				
	Greenville, NC, USA	●	●	●	●
	Toronto, ON, Canada				
	Whitby, ON, Canada				
	Manatí, Puerto Rico				
EUROPE	Bourgoin, France				
	Monza, Italy	●	●	●	●
	Ferentino, Italy	●	●		
	Milton Park, UK				
	Swindon*, UK				
	Tilburg, Netherlands				

* Our Swindon site is a condominium site that builds customized facilities to meet client needs for a variety of dosage forms.

Pharma services packaging capabilities

		STERILES			AUTO-INJECTOR	SERIALIZATION
		Prefilled syringe assembly	Syringe labeling and packaging	Vial/ampoule labeling and packaging	Assembly and packaging	
NORTH AMERICA	Allentown, PA, USA	●	●	●	●	●
	Cincinnati, OH, USA					●
	Greenville, NC, USA	●		●		●
	Toronto, ON, Canada					●
	Whitby, ON, Canada					●
	Manatí, Puerto Rico					●
EUROPE	Bourgoin, France					●
	Monza, Italy	●		●		●
	Ferentino, Italy			●		●
	Horsham, UK	●		●	●	●

LYOPHILIZATION DEVELOPMENT AND OPTIMIZATION

Simplify your process and produce stability within your drug product

Lyophilization can help overcome many of the quality challenges associated with complex, sensitive molecules, resulting in a longer shelf life for your drug product. Leveraging lyophilization development and optimization within early development provides foundations for a consistent, reproducible manufacturing process and ensures a cycle that is transferable to and compatible with GMP production-scale equipment while minimizing rejection rates.

"The QC group is very experienced and consistently delivers high-quality data and reports."

—Biotechnology company, USA

TECHNOLOGY TRANSFER

Simplifying the complexity of tech transfers and validation with a flexible, customized approach

Technology transfers are a crucial aspect of the drug product development process and can be quite complex. Each has its own unique challenges and requires a flexible approach. That's why you need a highly experienced partner who can help execute tech transfers quickly and effectively to keep your timelines on track, preserve your product supply, and reduce your program costs and risks.

Benefit from our proven technical transfer and process validation expertise. As your dedicated partner, we ensure:

- Process validation is in accordance with regulatory and cGMP guidelines
- Seamless execution for right-the-first-time delivery
- Access to a robust system to manage the product lifecycle
- Insight into all stage gates required for each phase
- Access to stability studies, analytical data, release testing, and other regulatory documentation

Navigating today's complex regulatory environment

Navigating the complex regulatory process of drug development today can be challenging, but it is vital to the success of your molecule. Our regulatory experts have managed regulatory submissions in more than 180 countries and will work hand in hand with you to build a robust and flexible regulatory strategy and proactively address your large molecule's unique needs and challenges.

Leverage our integrated regulatory solutions to:

- Access a range of CMC regulatory services for all product types manufactured across sites
- Support ICH Common Technical Document (CTD) Quality/Module 3 for clinical and commercial applications and lifecycle maintenance
- Support multi-jurisdictions such as those in the US, EU, and Canada, as well as international/ rest-of-world registrations
- Provide deliverables that are in alignment with the latest regulatory standards

INNOVATION: MYSUPPLY

Simplifying a complex supply chain

Mysupply is an end-to-end digital supply chain platform that provides visibility and enhances collaboration across the full product lifecycle. The mysupply platform can help you mitigate risk and keep you informed of production status by highlighting where and when your attention is needed most.

The mysupply platform provides near–real-time data sharing to enhance transparency, build trust, and encourage collaboration. Features include:

- **Forecasts:** Automated forecast entry and upload with status tracking capabilities to monitor progress
- **Orders:** Dynamic order submission and tracking capabilities detailing order-to-batch connection
- **Batch tracker:** Improved visibility into batch tracking and status for specific orders
- **Dashboard:** Up-to-date, transparent data for collaborative business reviews and daily performance management

Clinical trials

CLINICAL TRIAL SOLUTIONS

Mitigate your risk by leveraging our global network and supply chain expertise

For more than 30 years, Thermo Fisher Scientific has been committed to helping customers of all sizes develop comprehensive clinical supply plans that incorporate the need for flexibility in trial execution with a balanced risk and cost approach. From complete clinical supply plans to comparator sourcing strategies, distribution strategies, and package design recommendations, our experts are on hand to meet all your strategic planning requirements.

Our clinical trial solutions have a proven track record of working to mitigate supply chain risk, reduce cycle time, and deliver the right drug to the right patient on time, in full, and without compromise.

CLINICAL TRIAL MATERIALS

As you pursue regulatory approval, you will have access to high-quality clinical trial materials that are tailored to fit your needs and scope of work. Regardless of size, phase, or therapeutic area, we can provide efficient solutions for primary or secondary packaging, logistics, comparator, ancillary sourcing, storage, and distribution.

We also offer import/export services, including Importer of Record (IOR) capability in more than 25 countries to date, and best-in-class direct-to-patient services.

CLINICAL TRIAL SERVICES

With unwavering dedication to serving clinical research and patients around the world, we are powered by people with an exceptional commitment to delivering end-to-end, high-quality global clinical supply chain services.

We offer a broad range of clinical trial services that include:

- **Clinical trial packaging and storage**
- **Cold chain storage and logistics**
- **Distribution and logistics**
- **Clinical ancillary management**

Our solutions give you access to strategies and resources that will enable assurance of supply within your clinical trial.

COMMERCIAL PACKAGING

We have packaging lines throughout our global network, with the flexibility to support small or large volumes. Our experience and expertise add value throughout the packaging lifecycle. Our broad capabilities include vial, ampoule, syringe, and kit assembly.

Contact us now to learn about our end-to-end development capabilities for your large molecule.

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