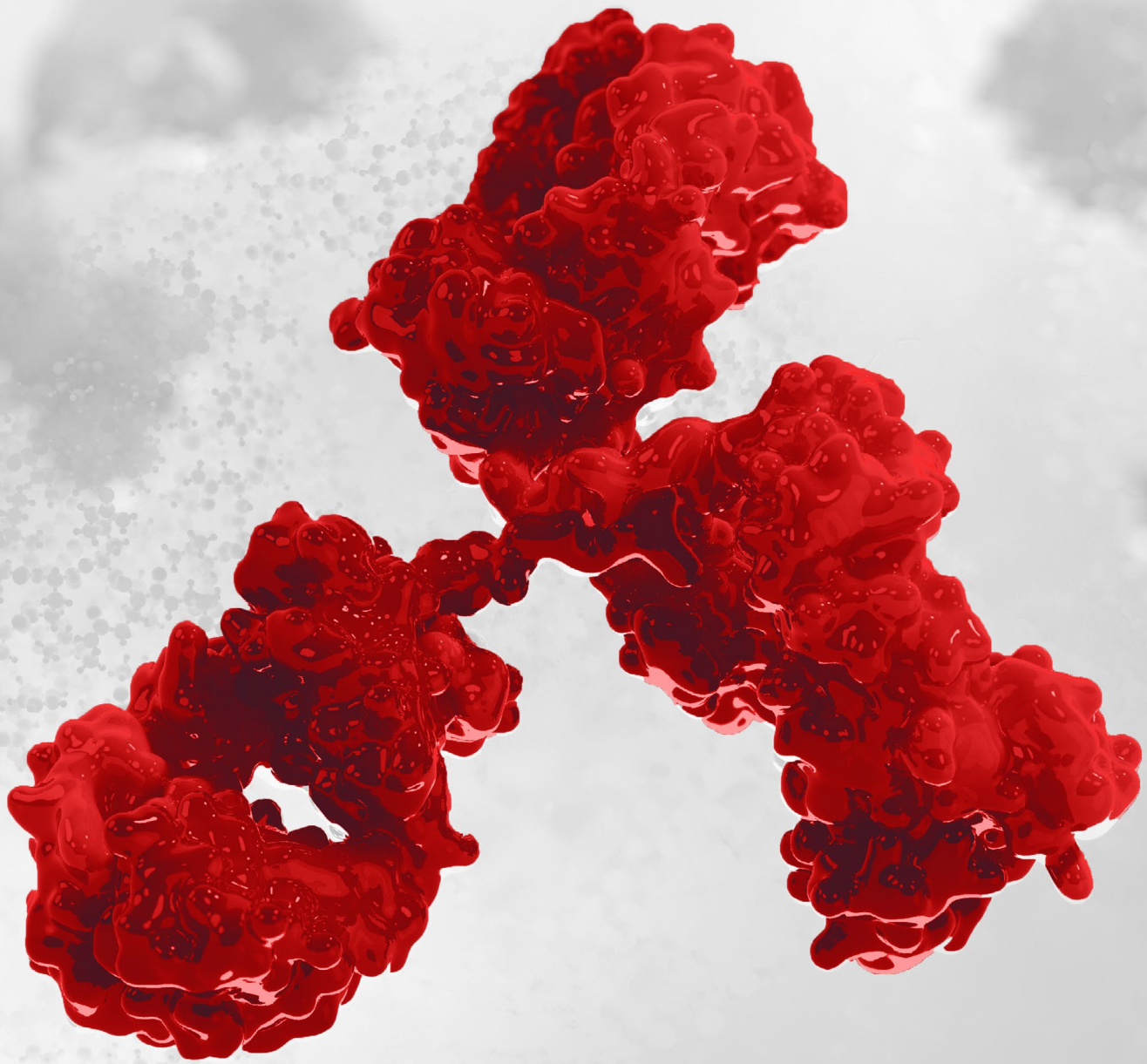
ThermoFisher SCIENTIFIC



Biologics

Large molecule development through manufacturing

Prioritizing speed and flexibility without compromising quality

How a small startup was able to scale up, without losing their precious material

Thermo Fisher was faced with a common challenge, that often comes without a resolution that maintains speed and flexibility. The dilemma: How can we quickly scale production of a large molecule, while keeping costs down, knowing that we will be starting with a low quantity of molecule. And the stakes were high. The client had already spent substantial 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. Thermo Fisher knew this process needed to be perfect. So, our team worked tirelessly to find ways to improve the cell culture performance, examining key process parameters and even completing additional process optimization steps to ensure success. The result: A flawless scale-up and, most importantly, a potentially breakthrough drug that was able to get into the clinic.

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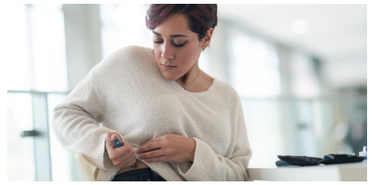
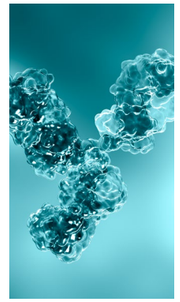




One partner. Fully connected.

Supporting you all the way, from development to commercialization

The demand for biologics continues to increase at an unprecedented rate, leaving no room for failure. You need a partner you can rely on to help successfully bring your drug to market reliably, efficiently, and on time.

Thermo Fisher Pharma Services is a full-service contract development and manufacturing organization (CDMO) and clinical research organization (CRO) that has the expertise and breadth of capabilities to seamlessly execute 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 strategic solutions, customized to your unique molecule and goals, from drug substance and drug product to clinical trials and commercial manufacturing.

Your biologic. Our expertise.

Position your molecule for success

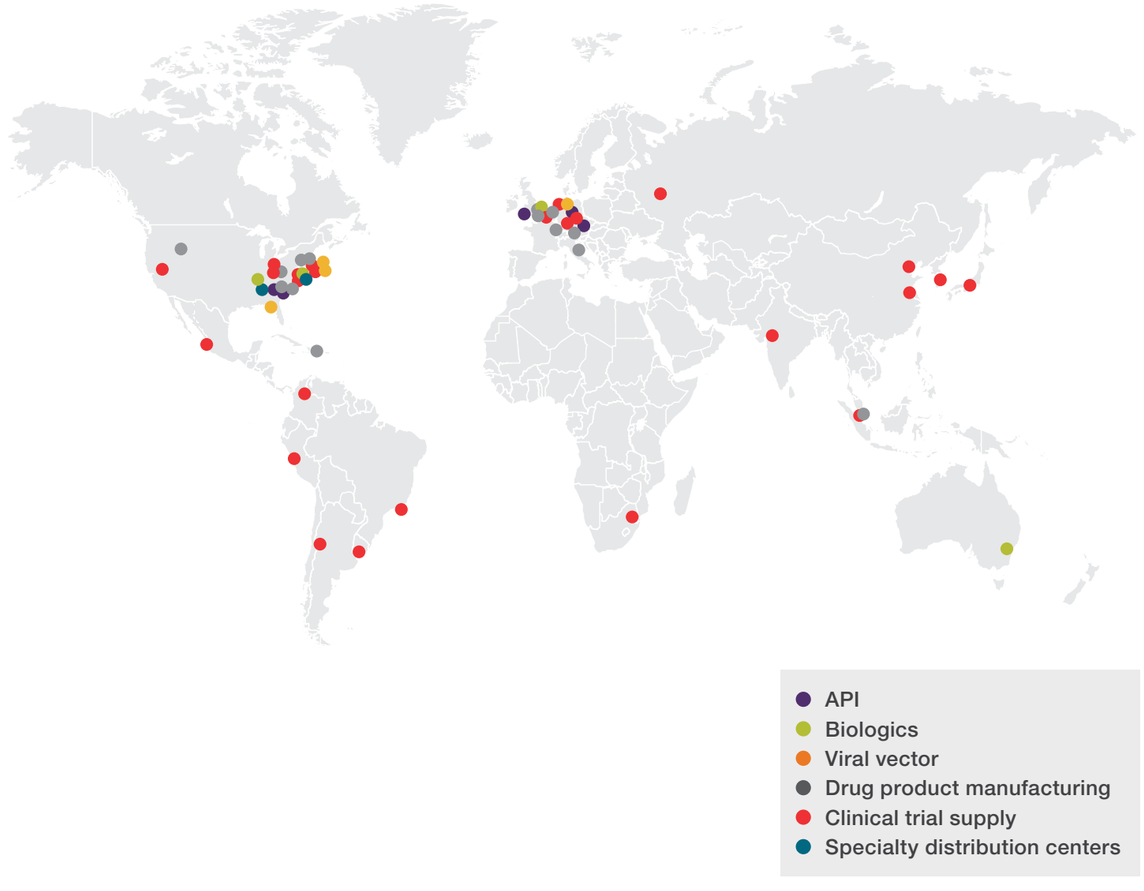
Our integrated end-to-end solutions are flexible and completely customizable to your large molecule. By partnering with a single vendor, you can remove complexity and bring your large molecule to market quickly, with lower cost and reduced risk.

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 quickly overcome any challenge—from complex molecules to regulatory hurdles to large-scale manufacturing.

Leave the complexity to molecules, simplify your development strategy with us.

We have an expansive global network of over 65 sites across 5 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.



Biologic drug substance

Large molecule drug substance solutions

Solutions to support the full lifecycle of your large molecule biologics

From cell line development through preclinical and clinical manufacturing and commercialization, our global network of experts understand the long and complex development journey and are committed to creating a tailored strategy, starting at any phase of the journey, to help provide you with a successful drug product ready for commercial success.

Utilizing innovative technology and equipment, including AI/ML for gene optimization, transpose technology and CHO-K1 for cell line development, and single-use bioreactors for pilot and large-scale manufacturing, we are able to significantly increase the batch yield, accelerating your time to market with a biologic that meets market needs. Our proven track record of scaling up biologics helps provide you with cost and time savings at every stage of development. Our experience working with new large molecule projects allows us to expertly handle any challenges your molecule can present.

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:

- Increased optimization through AI- and ML-based gene sequence optimization and vector construction
- Transposase-based technology in CHO-K1 cell line helps to enable speed to IND
- Guidance and collaboration throughout your journey from genes to final clone
- State-of-the-art, automated high-throughput equipment including Beacon™ system, Ambr™ 250 system, and Tecan™ platforms
- Platform seed train, fed-batch production, and harvest process
- Custom cell line development: use of custom or commercial cell lines, including CHO, myeloma, hybridoma, and PER.C6™ cells
- Simple cell line licensing agreements that avoid royalties or restrictions
- Regulatory guidance and support
- cGMP cell banking services
- Clone and media/feed screening, process development/ optimization using the Ambr 250 system
- Master cell banking
- Fed-batch, perfusion, and XD™ cell culture process
- Use of high-density mammalian cell culture technologies, including proprietary XD™ technology
- Cell culture process modeling, metabolite, and amino acid analysis
- Single-use scale-up and scale-down models
- Upstream process intensification
- Technology transfer
- Process characterization and validation studies
- Process robustness studies
- Design of experimentation (DoE)
- Process development, transfer, and optimization
- Scale-up from benchtop to commercial scale
- Chromatography—pilot and benchtop scale
- High-throughput screening and filtration
- Open lab analytical testing
- Material generation for studies
- Viral clearance studies
- Process characterization and validation studies
- Process robustness studies

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

Our robust and reliable biologics manufacturing processes are completed under cGMP conditions, utilizing our single-use bioreactors (S.U.B.s), which enables us to quickly and easily flex capacity and scale of your therapeutic as market demand fluctuates. With access to our technical experts, you can navigate late-stage with confidence and the ability to speak directly with our experts for guidance or to ensure your program's success.

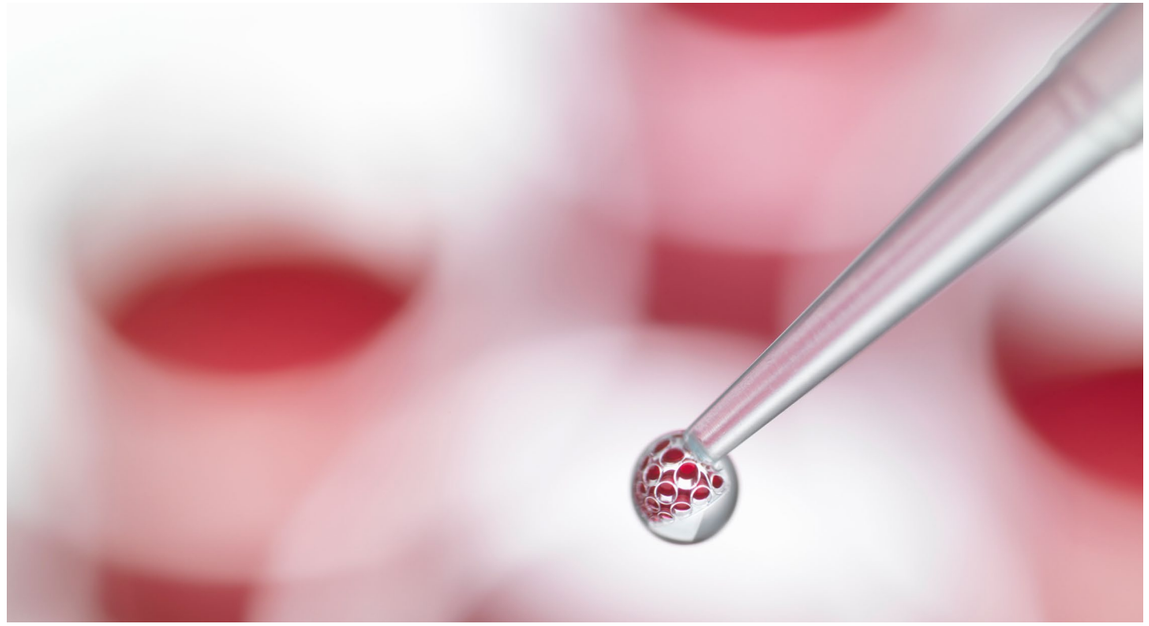
As part of the establishment of your commercial supply of biologic drug substance, we provide comprehensive services, delivering a final drug substance or drug product that adheres to regulatory and cGMP guidelines including:

- 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, US

Additional resources

- Large molecule drug substance solutions
- Upstream processing solutions
- Downstream processing solutions



Path to IND for biologics

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 Path to IND for biologics solution is an innovative platform developed to help shorten the time from transfection to IND to as little as 9 months.* The Path to IND 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	Manage risk	Prepare for long-term success
Shorten your early development phase to as little as 9 months* from the start of transfection to IND with best-in-class technologies, allowing you to file more quickly and secure funding.	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.	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.
• Cell line development • Cell culture and purification processes • Liquid-filled vial drug product formulation	• Analytical methods • Early non-GMP material for toxicology studies	• Released GMP drug substance • Released GMP drug product • Viral clearance and stability study data

"Exceptional speed and responsiveness."

– Biotechnology company focused on oncology, US

Additional resource

Path to IND for biologics

Path to IND for IgG1- and IgG4-based biologics

Timeline	What you provide	What we use	What we do	What you get
Option 1				
DNA to drug product (DP) release in as few as 9 months*	DNA sequence/gene	• Transposase technology in CHO-K1 GS knockdown cell line system, along with platform process, formulation, and analytics using commercially available raw materials.	• Cell line development	• **Early non-GLP toxicology material** • **Released drug substance** • **Released drug product** • **Stability data for IND** • **Templated quality-reviewed reports** • **Clinical trial packaging and labeling**
Option 2			**Plus ↓**	
Research cell bank (RCB) to drug product (DP) release in as few as 12 months*	RCB of stable pool or final clone	• Your cell line RCB, media/feed strategy*, and cell stability data. • Our platform process, as well as formulation and analytics development.	• Evaluation of our platform process • Platform formulation • Analytical methods • Toxicology batch • cGMP batch at any scale • Validation and characterization study • Stability testing	

Path to IND for bispecific and Fc-fusion-based biologics

Timeline	What you provide	What we use	What we do	What you get
Option 1				
DNA to drug product (DP) release in as few as 13 months*	DNA sequence/gene	• Transposase technology in CHO-K1 GS knockdown cell line system, and our platform processes and analytics with commercially available raw materials.	• Cell line development	• **Early non-GLP toxicology material** • **Released drug substance (DS)** • **Released drug product (DP)** • **Stability data for IND** • **Templated, quality-reviewed reports** • **Clinical trial packaging and labeling**
Option 2			**Plus ↓**	
Research cell bank (RCB) to drug product (DP) release in as few as 14 months*	RCB of stable pool or final clone	• Your cell line RCB, media/feed strategy*, and cell stability data. • Our platform processes and analytics with commercially available raw materials.	• Evaluation of our platform process • Formulation development • Platform analytical method development • Custom analytical method development • Toxicology batch • cGMP batch at any scale • Stability testing	

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.

We have extensive sterile injectable product development and manufacturing capabilities at all scales across our 8 clinical lines. 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 prefilled syringes and cartridges. We have an extensive record of sterile drug product commercialization success for our customers. 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 and commercial manufacturing capabilities

We provide both clinical- and commercial-scale capabilities at our six facilities located across three continents. Our team has more than 30 years of experience developing, optimizing, and scaling up bioprocesses for clinical and commercial cGMP manufacturing. With 24 commercial lines, nearly 1,000 m^2 of lyophilization capacity, and full formulation and process development capabilities at nearly all sites, scaling up is fast and seamless.

Thermo Fisher supported 65 steriles product approvals including 26 injectable NMEs from 2022 to 2024.

Thermo Fisher produced 491 million sterile vials and 127 million sterile PFS units (commercial and clinical) from 2022 to 2024.

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 products (different drugs) and provide complete fill and finish services for parenteral drug manufacturing, including liquid and lyophilized products in vials, prefilled syringes, and cartridges.

New capabilities are continually being added. A detailed list of current capabilities can be made available on request.

Sterile dosage forms, commercial and development

	Development				Commercial				
	Greenville, NC, US	Plainville, MA, US	Ferentino, IT	Monza, IT	Greenville, NC, US	Ferentino, IT	Monza, IT	Swindon, UK	Singapore
Liquid vials	2R–30R	0.5–10 mL CZ 2R–20R (glass)	0.5–100 mL	2R–100 mL	1–100 mL	2R–100 mL	2R–100 mL	2R–100 mL	2R–100 mL
Lyophilized vials	2R–30R		0.5–100 mL	2R–100 mL	1–100 mL	2R–100 mL	2R–50R	2R–50R	
Prefilled syringes and cartridges	1–10 mL		0.5–20 mL	0.5–20mL	1–20 mL	0.5–20mL	0.5–20mL		

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 standard.
5. New capabilities are continually being added. A detailed list of current capabilities can be made available on request.

A world of dosage forms

	North America		Europe			APAC
	Greenville, NC, US	Plainville, MA, US	Ferentino, IT	Monza, IT	Swindon, UK	Singapore
Liquid vials	✓	✓	✓	✓	✓	✓
Lyophilized vials	✓		✓	✓	✓	
Prefilled syringes and cartridges	✓		✓	✓		

Pharma services packaging capabilities

	North America		Europe		
	Allentown, PA, US	Greenville, NC, US	Ferentino, IT	Monza, IT	Horsham, UK
Prefilled syringe assembly	✓	✓		✓	✓
Syringe labeling and packaging	✓				
Vial/ampoule labeling and packaging	✓	✓	✓	✓	✓
Assembly and packaging	✓				✓

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.

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 help 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

Thermo Fisher supported 61 inspections resulting in GMP certificate and/or satisfactory GMP compliance status.

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 including: presubmission meetings, dossier prep, gap analysis, liaison support, and training
- 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 registrations
- Provide deliverables that are in alignment with the latest regulatory standards

Innovation: mysupply

Simplifying a complex supply chain

The mysupply platform is an end-to-end digital supply chain solution 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 trials solutions

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

For more than 30 years, Thermo Fisher 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 exceptional 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.

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

*** Terms and conditions:** Titer levels provided are estimates based on third-party results and may vary depending on molecule type or other factors. The timeline from DNA to drug product and the start of clinical trials for all Path to IND for biologics options may vary depending on molecule type or other factors and are estimates to be finalized once third-party cell line development dates are available and confirmed. The 9-month timeline involves additional risk.

Learn more at **thermofisher.com/patheon**
or email us at **pharmaservices@thermofisher.com**