ThermoFisher SCIENTIFIC

LARGE MOLECULE BIOLOGICS

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

patheon

HOW A SMALL STARTUP SCALED UP, WITHOUT SACRIFICING MATERIAL.

Jeff faced a dilemma: how to complete a large biomanufacturing scale up with the 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.

Comprehensive development & clinical manufacturing

Biopharmaceuticals now make up >40% of all the drugs currently in development. Plus, this combination of robust demand and limited capacity drives the urgent need to expand capacity. To address the growing marketing and your needs, Thermo Fisher Scientific is continuously investing in state-of-the-art technology and capacity expansions across our pharma services global network.[1]

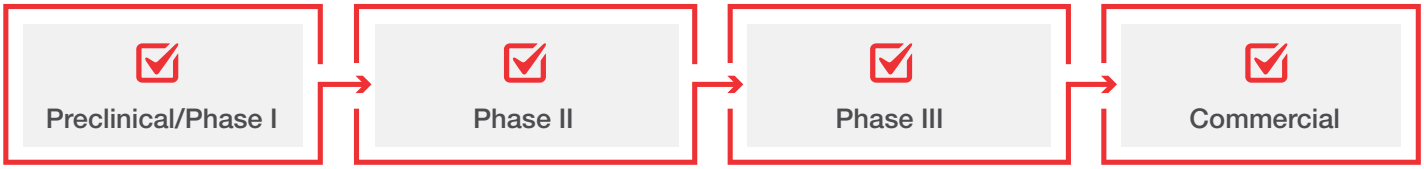
In addition to investing in capacity and technology, we invest in people and knowledge. Our network of biologics experts bring deep scientific expertise at every stage, helping you address immediate needs and prepare for long-term success.

Meeting your unique molecule needs

You need speed, flexibility, and often the perfect balance of both to meet critical milestones. We can help. Our experts offer strategic guidance and are prepared to find the right solution for your challenge, be it a custom build solution or something right out of the box.

Like you, we're driven by science and backed by a proven track record of scaling up biologics, ensuring you gain cost and time savings wherever possible. From preclinical to commercial production, our global network of experts understands the long and complex large molecule journey and are committed to help speed your molecule through early phase trials and prepare you for commercial success faster.

Supporting you every step of the way



FLEXIBLE SOLUTIONS CUSTOM BUILT ON EXPERIENCE AND EXPERTISE

Large molecule drug substance development requires a trusted partner that understands your unique and complex needs. Our global network of scientific experts provides expertise and enables end-to-end solutions for your drug development and commercial manufacturing needs. Our large molecule offerings include drug substance, drug product, and clinical trials supply solutions that support early development into commercial launch. You will have the option to work with one partner for both drug substance and drug product needs, improving decision-making and optimizing outcomes to ensure the success of your molecule.

To deliver on-time, we rely on standardized systems, processes, templates, and documentation. As one of the leading CDMOs for biologic drug substance, we also leverage everything we've learned from 650+ large molecule projects over the last three years. The average on-time delivery rate in 2019 was 90 percent.

"Great skill and leadership in manufacturing, program management, analytical, stability, etc."

— Biopharmaceutical company focused on auto-immune diseases, USA

[1]$170M invested in CapEx program from 2018-2023 across our St. Louis, MO and Groningen, NL facilities.

Enhanced Quick to Clinic™

Get the best from Thermo Fisher Scientific, even faster. With the newly enhanced Quick to Clinic™, you can balance timelines, risks and future needs on your journey to first-in-human trials.

Speed to milestones

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

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.

Build for success

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

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 Light Beacon® System • Evaluation of upstream and downstream platform process using high throughput automation technologies such as ambr® 15 microbioreactor & Tecan miniaturized purification platform • Formulation screening • Analytical method establishment & qualification • Toxicology batch • cGMP batch: 500L – 2000L • Viral clearance study • Stability testing	• Early toxicology material • Released drug substance • Released drug product • Minimum 1-month stability data for IND • Templated quality-reviewed reports • Clinical trial packaging and labeling (optional) • Regulatory CMC dossier for IND/IMPD filing

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

Upstream processing solutions

As a leader in manufacturing monoclonal antibodies and recombinant proteins using single-use technologies, our experts will provide you with upstream processing solutions that span across an integrated global network of cGMP facilities in Europe, North America, and Australia. Our expertise spans multiple commercial cell lines including CHO, and we specialize in fed-batch and perfusion cell culture processing. Solutions include:

- Fed batch processing—stable reliable production at titers >5 g/L
- Perfusion processing—high productivity and manufacture of unstable proteins
- Single-use technology—reduced technology transfer and scale-up risks, eliminate cross-contamination concerns

Downstream processing solutions

Our scientific experts will work to provide you a range of purification processes that ensures your drug substance is of the highest quality and yield. These processes include:

- Viral clearance studies
- Final product formulation
- Robustness studies

Learn more about our experience developing small and large molecules, including non-mAb biologics in this article.

Analytical solutions

We provide analytical solutions , including multi-attribute analysis (MAM), that include rapid identification and characterization of your recombinant protein or antibody, development and implementation of cGMP methodologies, and data generation for successful regulatory submissions. Analytical methods are developed in process development by the same teams that will use them in manufacturing to avoid delays and errors. Solutions include:

- Glycan profiling
- ELISA assays for product and impurity assessments
- Gel and capillary based electrophoresis
- Gel and capillary based isoelectric focusing
- Residual DNA detection
- Cell-based bioassays
- Imunologic and colorimetric assays
- Mass spectrometry
- ICH stability testing

Process validation

Our experts provide a complete validation package according to regulatory and cGMP guidelines, as part of the establishment of your commercial supply, in late clinical phases. These validations include:

- Validation of analytical methods
- ICH stability studies
- Container shipment studies
- CMC documentation in CTD format
- Process/product risk assessments
- Viral reduction studies
- Buffer and media hold studies
- Raw material criticality assessment
- Mixing qualification
- Filter validation
- Shipping qualification
- Freeze/thaw of bulk drug substance.

Manufacturing capabilities

We understand the unique needs of small companies—more than 74% of our clients are emerging and mid-size pharma/biopharma organizations. With more than 30 years of experience in early development and more than 20 years in process development, we provide a comprehensive end-to-end solution for all your large molecule drug substance development needs.

"For a small company, having a technically competent, customer focused team supporting us is critical to our success."

— Pharmaceutical company focused on women's health, USA

Global network for cGMP manufacturing

- All plants are flexible, multi-product facilities
- Platform equipment offering across sites
- Full life-cycle support from FIH to commercial
- Available footprint for capacity expansion

Extensive cell culture capacity

- 250L-2000L single-use disposable bioreactors available on all sites
- Thermo Scientific Hyperforma, Xcellerex, Sartorius systems 5000L
- DynaDrive bioreactors
- Cell line: mammalian
- Production modes: fed-batch, continuous perfusion, or XD®
- Globally 11 x cell culture suites available and >30,000L of production reactor volume

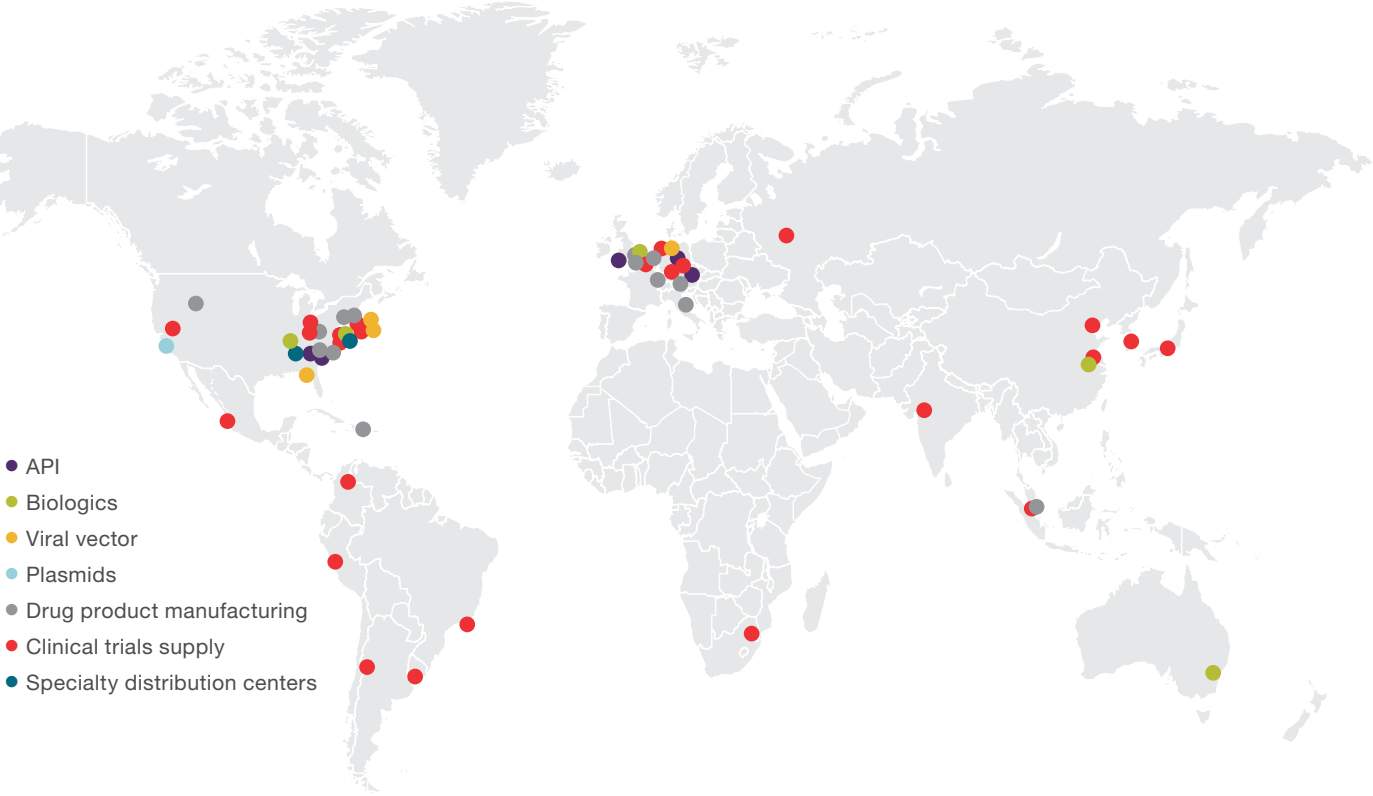
Flexible downstream capacity

- cGMP batch sizes of 100g – 20kg

DELIVERY EXCELLENCE

Our client-focused mindset and global expertise implement best-in-class, flexible biomanufacturing solutions aligned to your specific needs and position your molecule for greater success.

Integrated global network of technical, quality and customer engagement teams to support the drug development journey



18,000+
in 65+ sites

3,000+
scientists and engineers with deep technical expertise

3,700+
quality professionals

"Being a small company with limited resources, the Quick to Care program was a strong fit for us, because it allowed us to be able to manufacture across multiple sites while having the core program manager help us communicate and maintain relationships across the site to make sure that all the activities were completed under a tight timeline. One thing the Thermo Fisher team was very good at was understanding what our milestone was but also projecting what our next milestones would be."

— Kim Hocknell, VP, Technical Operations, Kaleido Biosciences

Integrated global network

Our integrated network of technical, quality, and customer engagement teams are ready to support your drug development journey. The Pharma Services network has 65+ sites across five continents and employs more than 3,000 scientists and engineers with deep technical expertise all working together to ensure the success of your molecule. We currently offer manufacturing locations in the United States, Europe, and Asia-Pacific, which provides you with simplified logistics and R&D tax advantages.

We offer a broad range of solutions that include:

- Clinical label services
- Clinical supply optimization
- Clinical trial packaging & storage
- Cold chain storage and logistics
- Distribution and logistics
- Clinical ancillary management

Our Quick to Care™ solution delivers a streamlined drug development program for your large molecule. The program combines your drug substance and drug product development, clinical manufacturing, forecasting, demand planning, and clinical trial supply execution into a single solution to help accelerate your discovery through clinical development.

Kaleido Biosciences, a clinical-stage healthcare company, approached Thermo Fisher asking for very individual approaches to their drug substance, drug product, and clinical trial packaging needs. These fragmented needs are what often drive smaller companies to work with multiple suppliers, stretching resources thin and ultimately adding considerable risk and time to the critical path of their molecule. Thermo Fisher was able to meet Kaleido's needs using the customizable and integrated Quick to Care™ program. Learn more here: **Kaleido Biosciences Successfully Meets Aggressive IND Filing Date Thanks to Strategic Partnership.**

"Cooperation, flexibility, transparency and diligence."

— Biotech company focused on oncology, Asia

"Great outcome and delivery of the batch to meet our material needs. The Brisbane site's willingness to take on the production with extremely tight timelines and ability to be flexible on this time-critical COVID-19 project."

— Research University, Australia

Dedicated global project management

Our experienced and dedicated global project managers have the expertise necessary to provide you with the process design that meets the needs of your discovery and your business. The assigned project manager will serve as the main point of contact between cross-functional teams, to provide you with a proactive, timely, and seamless approach to position your molecule for greater therapeutic and financial success.

Technology transfers done quickly and effectively

Whether you're scaling up or moving to another facility—we understand that as part of the normal course of business, technology transfers happen and vary in urgency. When planned for and executed correctly, technology transfers can lower manufacturing costs and improve robustness and efficiency. Our team of experts have the proven track record of delivering quick and effective executions to have your project back on track and preserve product supply as quickly as possible. Complete process validation in accordance with regulatory cGMP guidelines is critical to ensure the establishment of a reliable high-quality commercial supply, including:

- Process validation with critical parameters
- Validation of analytical assays
- Hold time studies
- Stability studies at required ICH conditions
- Container shipment studies
- Release testing
- CMC documentation in CTD format

181 tech transfers in 2020

92 drug substance, 37 development and 52 commercial

Industry-leading scientific and therapeutic expertise

We apply our large molecule biologics experience and therapeutic expertise to your discovery and execution strategy, to ensure we meet your unique needs and help increase the developmental and commercial success of your discovery. As industry leaders, we have the expertise in cell and gene therapy cold chain logistics, viral vector gene therapy and gene modified therapy manufacturing, and plasmid DNA manufacturing, in addition to being able to handle first generation biologics such as mAbs and recombinant proteins.

"This was a difficult legacy program where we (customer) did not have a lot of process/molecule knowledge. Despite the unknowns, Thermo Fisher successfully transferred the program and completed the GMP run on time and met specification."

— Biopharmaceutical company focused on cancer medicines, USA

SHAPING OUTCOMES

From development to commercialization, we provide our customers with the depth and breadth of innovative biologic end-to-end solutions. We apply a science-driven, risk-based approach to every step of the biologic development and manufacturing process, while providing you with a global footprint and the scientific and therapeutic expertise to ensure your discovery makes it to the patients who need it most.

Thermo Fisher Scientific works with you as a collaborative partner to mitigate risk and solve problems from biologic drug development to logistics. As your trusted biomanufacturing partner, we will help to simplify timelines and manage the increasing load of regulatory requirements while balancing cost in a constantly evolving market. We offer you a global network of drug substance and drug product facilities and experts, which can help you manage the unpredictability of forecasting and clinical supply chains. Thermo Fisher Scientific is the right partner—the first time.

+1 919 226 3200 ● thermofisher.com/patheon ● pharmaservices@thermofisher.com

Published 10/21

ThermoFisher SCIENTIFIC