

Scaling up manufacturing when it's needed most

Background

In early 2020, a global pharmaceutical company with an established relationship with Thermo Fisher Scientific engaged with our OEM and Commercial Supply team about supplying critical materials needed for the production of their SARS-CoV-2 mRNA therapeutic candidate. While the challenges related to SARS-CoV-2 were just beginning to take hold globally at this point, this company recognized the grave risk that SARS-CoV-2 posed. As such, they sought a partner that could ultimately help them produce millions of doses of their treatment (if approved) by supplying proportional amounts of nucleotides and all enzymes needed for mRNA production by *in vitro* transcription (IVT). Knowing this request amounts to a sudden and massive increase in raw material supply, the client brought this scale-up request directly to the OEM and Commercial Supply team at Thermo Fisher Scientific, knowing from past interactions that the team was well-versed in complex scale-up manufacturing and capable of building on experience to deliver when it mattered most.

Challenges

While scale-up capacity and experience have long been central to the manufacturing capabilities at Thermo Fisher Scientific, this particular request was unprecedented in size, scope, and delivery timeline. Due to the global spread of SARS-CoV-2, a major complication was that all RNA manufacturing components were needed as soon as possible, in order to produce a potential therapeutic intervention. This means all enzymes and nucleotides needed to be manufactured at appropriate scale simultaneously, rather than one by one, as is more common in traditional timelines. In effect, Thermo Fisher Scientific needed the processes and infrastructure to synthesize these critical components in parallel without interrupting existing manufacturing for countless other projects.



Capabilities

Capabilities at Thermo Fisher Scientific that power project success:

- A massive network of world-leading manufacturing sites staffed with interconnected and collaborative scientists, each with impressive experience executing unique and substantial scale-up projects
- Decades of manufacturing R&D and knowledge geared towards understanding expression systems and improving manufacturing processes to increase yields and material output for optimization of process scaling
- A complete portfolio of materials needed for mRNA synthesis (including animal origin-free reagents) and operational know-how for producing these specific materials at scale and in full regulatory and quality compliance

- Ability and willingness to invest in growing the number, size, and scope of manufacturing sites and their staff for the benefit of clients on the cutting edge of life sciences
- Proven ability to rapidly mobilize a devoted project team equipped to determine an overarching strategy, set an implementation path, and execute deliverables of projects with formidable scope and critical timelines

Partnership

Prior to this request, Thermo Fisher Scientific had served this client's OEM and commercial supply needs for approximately 8 years, helping them to quickly grow their business and expand their drug discovery and development pipelines to cover additional therapeutic areas. Through this highly effective partnership, Thermo Fisher Scientific repeatedly demonstrated a capacity to source both standard and custom manufacturing solutions, as well as a willingness to invest in the future of the collaboration. Recognizing how the commercial momentum of Thermo Fisher Scientific had already translated into their own success, this global pharmaceutical company understood that expanding this partnership could help them reach their aspirational goals, even during extraordinary times.

Results

- With an agreement in place, Thermo Fisher Scientific immediately went to work supplying Thermo Scientific™ TheraPure™ nucleotides and enzymes for early therapeutics development. Thermo Fisher Scientific was producing TheraPure nucleotides at intermediate scales with no infrastructure changes required. Production

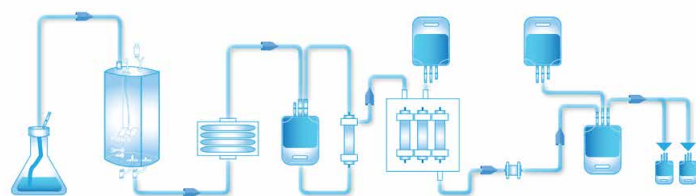


Figure 1. Schematic of a closed SUS-based process for enzyme manufacturing. The SUS and proprietary processes at Thermo Fisher Scientific help remove the risk of DNA contamination present in the conventional manufacturing process.

of IVT enzymes was previously operated exclusively at smaller, nonindustrial scales, which meant that manufacturing scientists needed to translate small-scale enzyme manufacturing processes to intermediate-scale single-use system (SUS) processes to further enable IVT enzyme production (Figure 1).

- Simultaneously, Thermo Fisher Scientific made a significant investment at the Biosciences Center for Excellence in Vilnius, Lithuania, electing to build a new 57,000 sq. ft. facility. Once completed, this facility could manufacture TheraPure enzymes and nucleotides at industrial-scale levels. In doing so, Thermo Fisher Scientific absorbed significant risk by investing in advance in order to ensure a future supply of raw materials to the client. Construction broke ground in May 2020 (Figure 2).
- As site planning and construction continued, Thermo Fisher Scientific hired over 150 full-time employees for manufacturing and site operation functions. Once the facility was built, the workforce installed state-of-the-art instrumentation and equipment, developed and verified industrial-scale manufacturing processes drawing on key R&D, and created a facility able to produce TheraPure products in full compliance with ISO 13485 quality management systems. By November 2020, the first commercial batches were being supplied to the client from this newly expanded site.
- Additionally, Thermo Fisher Scientific made further investments in other manufacturing locations, particularly building up the Center of Excellence for mRNA Vaccine Raw Material at the Milwaukee site, to add redundancy to nucleotide production and increase capacity.



Figure 2. Construction of the manufacturing site in Vilnius, Lithuania.

Summary

After formalizing an unprecedented agreement, Thermo Fisher Scientific drastically scaled up raw material manufacturing for mRNA production, leaning on many decades of experience. In ~10 months, this massive increase in manufacturing of critical nucleotides and IVT enzymes went from discussion to reality, meeting both client and public health needs. In total, our OEM and Commercial Supply team sourced raw materials for therapeutics candidates, from concept to clinical development and on to industrial-scale production, all while maintaining the highest quality standards. Importantly, the financial resources Thermo Fisher Scientific put to client use accelerated scale-up at a pace unheard of across the industry. As a result, the OEM and Commercial Supply team met the massive need of this pharmaceutical client while growing capacity to serve future partnerships within nucleic acid therapeutics.

About OEM and Commercial Supply

When partnering with the OEM and Commercial Supply team at Thermo Fisher Scientific, you gain access to the tremendous resources and knowledge assembled through a track record of successful partnerships and as a world-leading scientific organization.

In addition to accessing our broad product portfolio, a partnership with Thermo Fisher Scientific also helps ensure success through our effective and well-demonstrated problem-solving. Our OEM and Commercial Supply team has seen firsthand that every project has its own specific challenges, but significant infrastructure and a technical approach to manufacturing go a long way towards circumventing and overcoming both common and one-of-a-kind problems. To this end, our expansive worldwide network of sites is populated with research-oriented manufacturing scientists who leverage their previous experience to quickly identify and resolve issues.

Our team is devoted to clear and open communication—an essential aspect of maximizing efficiency and seamlessly solving problems. The commercialization team will provide immediate points of contact to act as your advocates, devoted to putting the full weight and resources of our world-leading organization behind your project at every step of the commercialization journey.

Find out more at thermofisher.com/oem

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