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Enabling Fast And Appropriate Drug Product Supply For Phase 1 Clinical Trials

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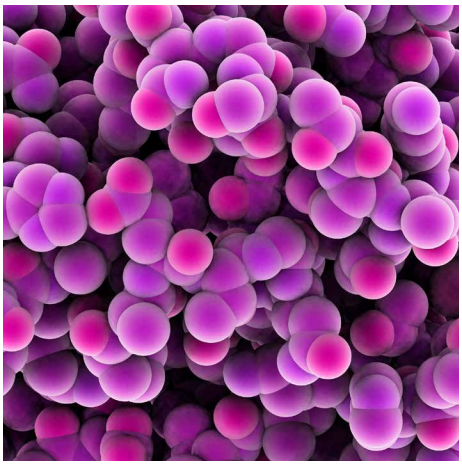
Reducing the timeline from conception to Phase 1 trials can be especially challenging for new and emerging biotechs. Since many of them are completely virtual or have limited lab space capabilities, they often do not have in-house resources and capacity for formulation development. Without the ability to move smoothly from lab concept to the manufacture and delivery of GMP clinical supplies to patients, critical milestones could be missed, potentially delaying funding commitments from investors.

This in-house capability gap has led to tremendous growth in the CDMO market, as more of these companies are turning to outsourcing for early-stage development. The partner you select must have highly skilled and experienced people who understand your process, can work to solve complex challenges, and will ensure your molecule and product are manufactured using the most robust and efficient processes. These advantages give you the speed and flexibility that is critical in early drug development while also establishing a clear path that takes you all the way to commercial success.

Securing the future of your molecule

The competitive landscape in early drug development is especially prominent in meeting unmet patient needs. In areas where there is a more urgent need to develop these orphan drugs, such as specific oncology and central nervous system indications, getting ahead means showing an efficacy signal as early in clinical development as possible. And while new and emerging biotechs are experts on the science of their disease focus, they often do not have the capabilities and industry experience to convert the concept into a high-quality drug substance and an appropriate and consistent dosage form. In addition, the target patient population is often more difficult to find around the globe, intensifying the need to understand regional regulatory requirements in multiple countries. It is important the drug product you make arrives at the clinical sites at the right time and intact (e.g. protected against high shipping temperatures) to support patient dosing requirements. Therefore, while the reward of a successful startup can be substantial, these ventures come with considerable risks and uncertainties.

Looking at the historical trend in R&D costs per approved compound (Figure 1), there has been a relentlessly upward trend in the cost to go from discovery to an approved product.



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Sources: 1970s, Hansen (1979); 1980s, DiMasi et al. (1991);
1990s-early 2000s, DiMasi et al. (2003); 2000s-early 2010s, DiMasi et al.

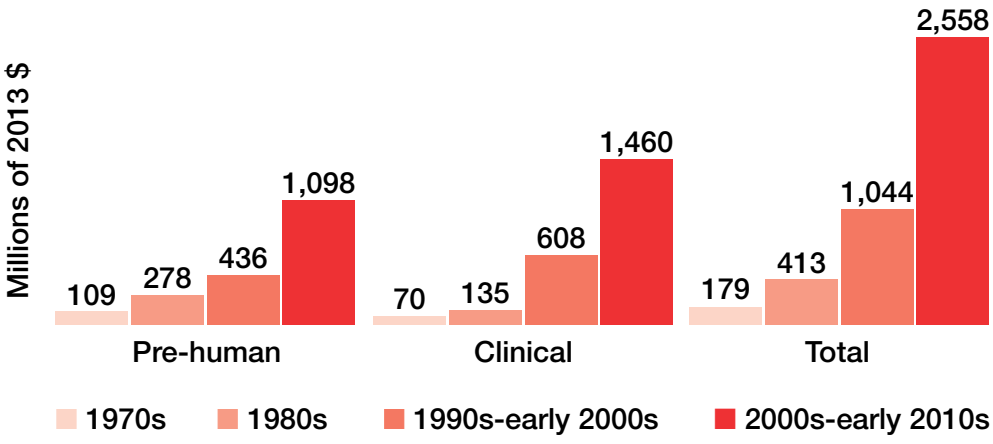


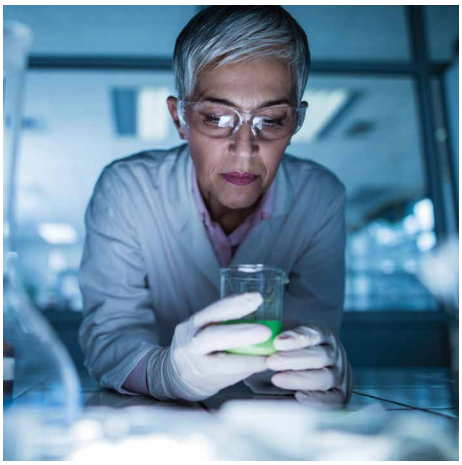
Figure 1: Historical trend in R&D cost per approved new compound

This challenge is exacerbated by the fact that only about 14 percent of all drugs in clinical trials eventually win approval from the FDA.1 For small drug companies pursuing a small molecule, this means they must beat their competitors to market with limited capital and a very small margin for error. Making it to Phase 2, where dose response and efficacy signals of a drug candidate can emerge, marks a milestone that gives venture capitalists investing in the program more confidence that they will see a return on their investment. Doing so, though, requires early mitigation of product development risks that can help avoid clinical trial failures later. This calls for a wide range of expertise, including extensive knowledge in chemistry, manufacturing, and controls (CMC); regulatory compliance; and clinical trial management – resources that are often limited or not available in start-up pharma companies. Outsourcing is often the solution to fill these gaps, but it is important to work with a CDMO that incorporates cross-functional communication.

For example, in Phase 1, the focus is on identifying safety and tolerability at various dose levels, which will then need to be evaluated for potential side effects. However, a CDMO should not simply convert powder into an arbitrary dosage form without knowing the target patient population and any nuances associated with the therapeutic indication. This involves open discussion with clinical operations in conjunction with CMC development requirements. Questions worth exploring may include weight dosing and titration, home administration or site needs, countries targeted to ensure qualified person support in advance, short- and long-term stability, and temperature requirements.

Recognizing the importance of aligning formulation, drug product manufacturing, and clinical trial management activities, Thermo Fisher Scientific developed the Quick to Clinic™ program.

Therefore, pharmaceutical scientists should be interacting with those in clinical trial supply to break down silos that could lead to inefficiencies and a slower path to clinic. Recognizing the importance of aligning formulation, drug product manufacturing, and clinical trial management activities, Thermo Fisher Scientific developed the Quick to Clinic™ program. This service is designed to reduce the timeline to deliver Phase 1 supplies using a wide range of resources so that new and emerging biotechs can meet the crucial milestones for their project without compromising quality.



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Quick to Clinic™ overview

The Thermo Fisher Scientific's Quick to Clinic™ program timeline (Figure. 2) is designed to have a Phase 1 drug product manufactured, labeled, packaged, and delivered to the clinic within 14 weeks of receiving a small molecule API.

Nevertheless, there are many factors to consider when converting a drug substance into a drug product. Phase-appropriate formulations offer the quickest path to clinic, but not all drug substances fit into the simplest clinical format. That is why the Quick to Clinic™ process begins at one of Thermo Fisher Scientific's standalone sites (located in Bend, OR, and Milton Park, UK) dedicated to early development of oral solid-dose products up to Phase 2. Here, the Thermo Fisher teams focus on ensuring they understand the physicochemical attributes of a molecule (e.g. low aqueous solubility) that may be problematic enough to require an enabling formulation. However, if the simplest format is appropriate, prototype batches are made – which can be API or blended powder in capsules or bottles – in only a couple of weeks to generate the stability data to support a regulatory filing. Verification of analytical methods is completed at the same time. Once GMP API is received, the drug product is manufactured and a one-month stability study for the bulk materials begins.

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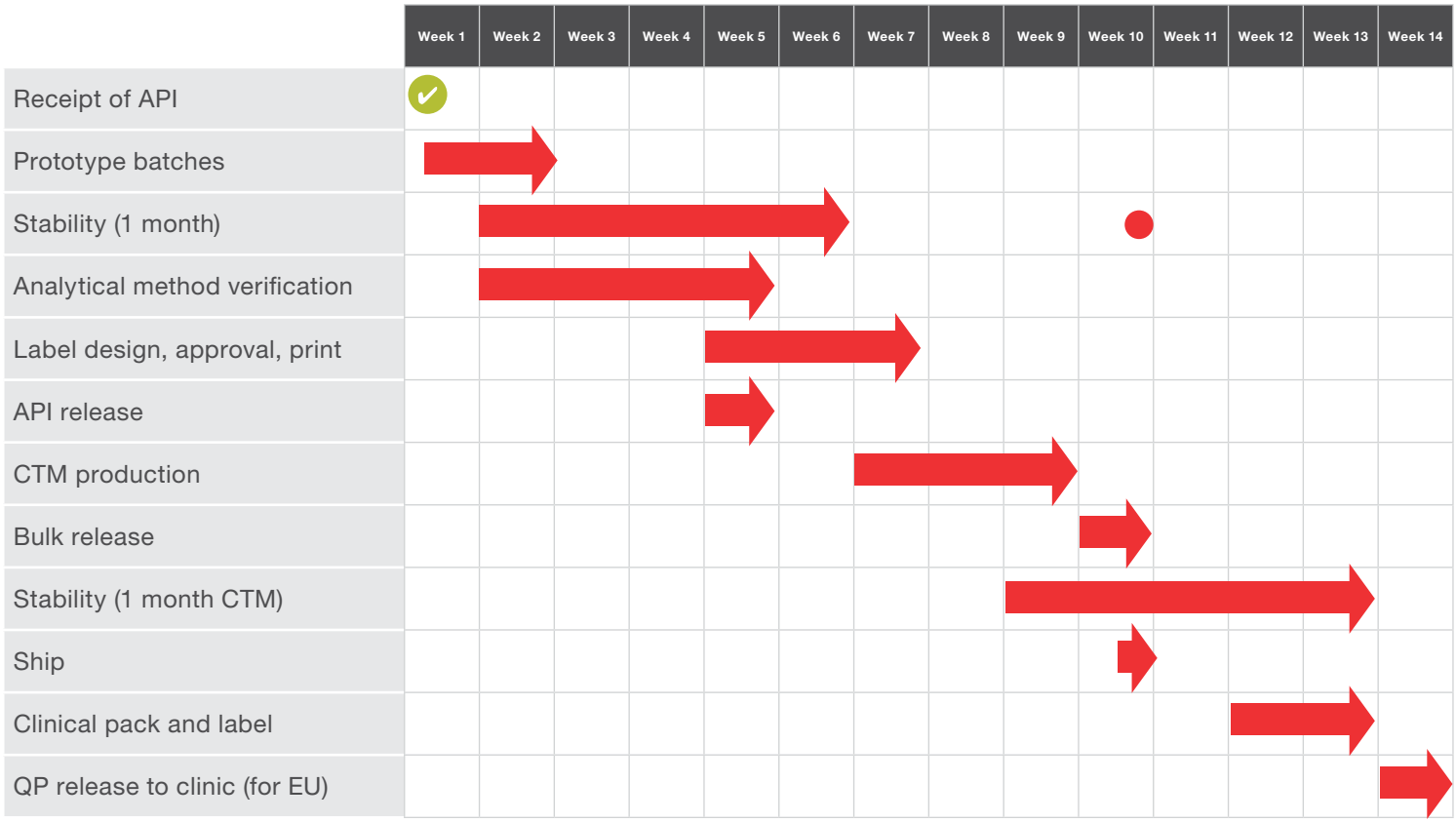

Figure 2: Thermo Fisher Scientific Quick to Clinic™ 14-week timeline

In parallel with formulation development activities, clinical supply chain experts from one of the Thermo Fisher Clinical Services sites (in the US or EU) review the overall clinical study requirements for packaging, labeling and distribution. A review of the clinical protocol will inform the design of the labels, which are approved by the client and then printed to be ready in advance of GMP manufacture. The bulk GMP materials released from the Bend or Milton Park drug product site are then shipped for clinical packaging and labeling. Dosing requirements can assist in identifying short-term packaging requirements in bottles or blisters and to further identify immediate and long-term stability requirements for the clinical phases. Due to active project management between the drug product and packaging teams and the use of a single project plan and timeline, the clinical trial management team can receive the details and requirements for the client's program sooner and outline a plan for clinical packaging and labeling based on that information. This includes risk-mitigation strategies based on potential scenarios to account for any possible interruptions or issues. Finally, in Week 14, Thermo Fisher Scientific can release and ship the properly packaged and labeled supplies to the client's clinical sites.

A Quick to Clinic™ case study

For one client, the strategic thinking of Thermo Fisher Scientific's Quick to Clinic™ allowed them to generate a proof of concept quickly, so they could deliver their product to patients, despite some surprises along the way. These included challenges with respect to the API supply, such as limited availability and differing physical properties between the non-GMP and GMP batches received. Subsequently, one batch of drug product in limited stock had to supply three different clinical studies. The team also had to propose one bespoke label design to accommodate these multiple studies using the same drug product, and, in addition, they identified a solution on short notice when the original packing materials were no longer available. However, as the Quick to Clinic™ strategy proactively uses process mapping to outline all potential workflows of a project and identify any possible risks, back-up plans were already in place, enabling the implementation of quick solutions. Therefore, Thermo Fisher Scientific and the client were prepared for these scenarios and were able to quickly respond to any documentation requests as a result, preventing any delays in the 14-week timeline.

One team, one voice

The seamless integration of Thermo Fisher Scientific's formulation and clinical management with Quick to Clinic™ sites means one team of experts. Fewer vendors for the client to manage reduces the time burden typically dedicated to coordinating different parties and locations, and it allows the sponsor to focus more on value-added activities within their organization. With open communication and a one-team approach between the drug product and clinical packaging teams, escalations are easier and faster, eliminating handover or loss of ownership during transitions. These benefits, combined with the expertise and resources within the Quick to Clinic™ program, offer a competitive edge that can help secure future funding, strengthen your process development, and, ultimately, improve the quality and safety of your product for the patients who need it.

References

1. CenterWatch. (2018). New MIT Study Puts Clinical Research Success Rate At 14 Percent. Retrieved from https://www.centerwatch.com/articles/12702-new-mit-study-puts-clinical-research-success-rate-at-14-percent#:~:text=New%20MIT%20Study%20Puts%20Clinical%20Research%20Success%20Rate%20at%2014%20Percent,-February%205%2C%202018&text=Nearly%2014%20percent%20of%20all,MIT%20Sloan%20School%20of%20Management.

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