White paper

Early development

Complex early development studies — managing FIH to phase Ib

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Early-phase clinical studies range from simple to complex, and all must be conducted rapidly while maintaining subject safety and data quality. They are also generally not performed in isolation, and they lay the foundation for future studies to further our understanding of drug metabolism and safety in support of a new drug candidate. Partnering with a trusted contract research organization (CRO) like the PPD™ clinical research business of Thermo Fisher Scientific enables our sponsors to benefit from decades of early-phase experience, extensive global reach, and broad service capabilities.

Our expertise spans across all development phases, offering a program solution to small biotech clients. We can offer the flexibility needed to apply evolving strategies to the management of early-phase studies involving novel medicines and ensure that sponsors have access to study strategies that will be optimal in terms of time, quality, and cost from early phase through to registration.

Start with understanding the study drivers

Early-phase first-in-human (FIH) or clinical pharmacology studies are conducted to understand the metabolism and safety of a new drug candidate. The goal is to ensure that the drug and the dosing regimen are safe and maximally efficient, while identifying potential biomarkers to provide insight into efficacy for later stage studies.

Every early-phase study is different, and each will always have very specific endpoints. Our job is to work with our sponsors to establish the key drivers for their study so we can build an effective strategy that supports their vision. For some clients, study cost may be the primary driver, but, in some situations where the study is on the critical path to a market application, delaying time to market would have much higher cost implications.

Understanding the forces behind early-phase studies helps a CRO develop a solution that best meets the sponsors' needs. Some sponsors have a fixed idea of process and outcome and are just looking for a CRO to provide a practical study design that delivers the study quickly and efficiently. In other situations, the overall future clinical development program timeline may be the corporate focus, therefore building into the phase I first-in-human study a patient cohort to provide early insight to proof of concept can help secure funding for future clinical development or inform clinical endpoints in later-phase study designs.

Then move to proper planning

Early-phase studies are just that—the first step in the clinical development process. For some, they lead to the next study on the way to getting a new drug product licensed/approved as quickly as possible. For others, like small biotechs, it may involve establishing proof of concept in order to attract investors or licensing partners. The best CROs, are ones that can bring to the table solutions for the entire development life cycle and treat these early-phase studies as part of a broader development program.

Risk management is an essential aspect of strategic planning for these studies and programs. Some sponsors like to be aggressive, taking risk with conducting studies and activities in parallel in order to move as quickly as possible, while others prefer the security of time and cost, with contingency planning included in fixed price for fixed-scope budgets. The former may not want to bother with any backup solutions; the latter may require additional backup options built in up front, which may comprise additional sites or cohorts.

We build a strategy according to the client's needs, risk tolerance, and expectations, leveraging our expertise and understanding of the complexities of the study design and the capabilities of the sites involved. The functional groups involved in each study establish risk-mitigation plans up front for potential problems that our project managers—through ongoing meetings with those groups—continually monitor based on the level of risk in order to trigger timely backup plans.

Communicate Effectively

Project managers are the experts in communication, ensuring timely and effective communication across functions and between stakeholders. They set clear expectations for timelines, interdependencies, and responsibilities. All team members must understand the implications of timeline shifts in their areas of responsibility for other downstream functions. Project managers establish communication plans from the start and appropriate escalation steps for each functional area so the entire project team can be notified appropriately in a timely manner. If issues become more urgent, the right senior leaders can be engaged immediately to help secure timely solutions.

Establish the Right Team

Upfront triage with an integrated team is also critical to the success of early-phase studies. That team should be constructed based on the elements that are important to the study and sponsor. For clients looking for proof of principle, engaging the later-phase team, particularly colleagues with therapeutic expertise, in the discussion is important.

Our development physicians assess each protocol and provide medical considerations based on their therapeutic indication expertise in consideration of the patient population and the endpoints that need to be factored into a study to ensure the best strategy to deliver results, consistent with standard of care. Having representation from site principal investigators in different regions, even if some of the sites may not enroll many patients, provides an opportunity to get the endorsement of additional key opinion leaders and ensure consistency with standard of care across regions and patient types.

Our team includes lab and pharmacokinetic experts, ensuring that suitably validated assays are used to make effective go/no-go decisions at early stages in a program. Including global team members on the early-phase study teams is also recommended for candidates for which sponsors will ultimately be seeking global registrations. These experts can help ensure that endpoints for the study will meet regulatory acceptance across the world.

Expect Change

While there is a standard set of clinical study designs that are predictable and consistent in early-phase studies, there are often unique challenges arising from rapid timeline expectations. As a result, systems, processes, and ensuring teams have the flexibility to adapt quickly to change are key to success and to ensure that solutions are customized for each client and opportunity in order to manage speed while ensuring the quality of the study outputs. Experts with the right mindset who understand the expectations and can work flexibly when problems arise are essential, as are pre-developed solutions that can be readily implemented.

Traditionally, an early-phase, single ascending-dose study was followed by a multiple ascending-dose study, both in healthy volunteers. Today, it is possible to add a patient arm in order to understand the drug safety and potential efficacy in the intended patient population. This arm also provides some initial indications of biomarker relevance. Adding these patient arms early in the study design while carefully monitoring safety signals helps facilitate rapid progression to phase II/III.

We have the expertise and skill to bring patients into early study designs, dose them, look at the safety data, and then increase the dose and expand to more subjects safely. We recommend this strategy with many clients, particularly small biotechs, so they can provide their investors with early proof-of-concept data.

Leverage Broad Systems to Form Deep Partnerships

For early-phase studies that are part of a program designed to result in a new drug product approval, it is important for the CRO to have systems in place that provide a portfolio view of each study within the overall program. Both the early-phase and late-phase teams need to have an understanding of where the studies they are involved in are on the critical path to an overall submission timeline.

Our systems and processes enable the necessary understanding of sponsor goals and provide the appropriate level of oversight and management. Combined with our approach to program performance management and commitment to communication,

Expediting the Clinical Development Process

Regulatory acceptance of study designs that expedite the clinical development process has increased, particularly following the COVID-19 pandemic. Study designs are evolving to more often include early clinical proof of concept, resulting in an explosion of therapeutic phase Ib studies. The goal is to ensure that all the right data are collected as early as possible in clinical development and not that a specific series of studies is conducted.

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we can help clients identify the right development pathway and stay on track. For small biotechs, we are able to supplement their teams with expert resources in each function or region to provide a wealth of skills and experience to match any large pharmaceutical company. When clients partner with us through our program approach, they benefit from our consultancy services, strategic and regulatory guidance, global out-reach, and breadth of experience that is not possible to afford on an individual study basis.

The support we provided to companies developing COVID-19 therapies and vaccines is a great example of bending the time–cost curve to achieve sponsor and public health goals. Going from concept to a licensed vaccine in less than 12 months could not have been possible without a robust CRO/sponsor partnership and a joint commitment to expediting the clinical development strategy. Rather than separate phase I, II, and III studies, we worked with clients and regulators to ensure early clinical endpoints to inform later-phase studies and achieve seamless transition across formal phase I–II/III study phases using combined protocols. The expedited timelines and parallel development approach could not have been achieved without working with a single CRO that can provide all of those services in a programmatic fashion

Global reach, experience, expertise and integrated support

Our early development services team are often the first interaction a client has and serves as integrators to the broad range of services we offer. We can help with project management, lab analysis, and building a clinical development plan across phases and regions. As a multi-solution provider, we support sponsors with everything they need to bring their products to market—and beyond.

We are also equipped to take on entirely new projects, which we demonstrated during COVID-19. We are able to align our experience with problems arising from the pandemic and develop optimum solutions. We can tackle treatments for new rare genetic diseases and studies involving novel drugs with first-in-class mechanisms of action. Providing strategic guidance on clinical development is a core skill set and a differentiator for us. In addition, our experience, combined with our relationships with 30 partner sites in all regions across multiple countries, makes it possible to build the best possible strategies for sponsors in terms of time, quality, and cost. We are a trusted partner that adeptly delivers results in any indication.

Learn more at **ppd.com/our-solutions/clinical/early-phase-clinical-trials/**