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The perils of building clinical trials on a shaky foundation

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Average overall likelihood of approval by the Food and Drug Administration for investigational drugs entering Phase 1 studies is a mere 9.6% — effectively a one in 10 chance of those treatments entering the market. This low success rate is extremely problematic and concerning to industry stakeholders, not to mention patients waiting on the sidelines.

Adding to this dilemma is the growing complexity of clinical trials. According to a report by the Tufts Center for the Study of Drug Development, the average study protocol now includes 13 endpoints, 167 procedures, 35 inclusion and exclusion criteria, and requirements for 11 site visits per patient over a 175-day period, resulting in a dramatic increase in study costs. Oncology trials have the highest per-patient cost of any therapeutic area, averaging $59,500, with other therapeutic areas averaging $36,500 per patient.

With the advent of highly targeted therapies in oncology, pharmaceutical companies are faced with supporting an ever-growing number of studies that require fewer participants, meaning fixed costs are spread out over a smaller pool.

With spiraling costs and increasing stakeholder demands, it is critical that studies get off to the right start, in terms of patient selection and recruitment. This is self-evident for pharmaceutical companies needing to remain competitive, allowing them to scale the number of new drug candidates in their pipeline — particularly for complex therapeutic areas such as oncology and central nervous system. But how do we get there?

No silver bullet

As with any complex challenge, multiple solutions have been proposed to address these root causes, however, there is no single silver bullet that will accelerate clinical trials. Fully optimizing the clinical trials process requires practices and tools that streamline operations, automate processes, increase visibility and improve collaboration with pharma, contract research organizations (CROs), sites, regulators and review boards.

A recent publication in the Journal for Clinical Studies offered a solution for mitigating highly complex and specialized protocols: leveraging CROs and research staff who are more therapeutically aligned. This involves finding study staff with the right mix of technical as well as therapeutic expertise for making the specialized assessments necessary to measure certain endpoints.

Others point to the use of biomarkers as a potential avenue for delivering higher success rates. A recent editorial from the chief medical officer at Definiens offered a simple explanation for the high failure rates in clinical research: the lack of biomarker discovery and implementation across the industry. A recent study from BIO found that rare disease programs and programs that utilized selection biomarkers had higher success rates at each phase of development compared with the overall dataset. The idea is that selective biomarkers can be used in various ways to increase the likelihood of success and reduce costs. Validated biomarkers can be used to do everything from identifying the efficacy early in drug candidates to increasing the measurement precision used in inclusion or exclusion criteria for enrolling patients into clinical trials - resulting in eliminating bad drug candidates sooner and more precise patient selection.

In areas where surrogate biomarkers are harder to identify (such as CNS) some have focused on innovative study designs and clinical surveillance on signal detection as tools for enacting a meaningful enhancement of the current research paradigms.

Ultimately, the entire ecosystem needs an overhaul and today pharmaceutical companies have access to a variety of cloud-based technologies that can radically improve the clinical trials process.

Getting back to the basics

Though it is certain that the issues are complex and challenges differ across therapeutic areas, the fact remains that the complexity of clinical research continues to grow, a confluence of globalization, outsourcing, protocol complexities or ever-increasing regulatory mandates. The common denominator and foundation upon which clinical research is successfully initiated is the study startup (SSU) process.

SSU is a complex business, composed of country selection, pre-study visits, site selection and initiation, regulatory document submission, budget and contract negotiations, patient recruitment initiatives and enrolling the first patient.

When that foundation is poorly built, timely re-work may be required or worse — the study may need to be rescued or abandoned altogether. There are multiple elements to this foundation which need to be orchestrated simultaneously to be successful, which amounts to a challenging balancing act. Signals that your trial is not on solid ground may include:

- Poorly selected sites that are struggling with enrollment/retention of trial subjects
- Little oversight or transparency with CRO partners
- Lack of robust risk identification and management processes
- No benchmarking metrics to gauge progress against or upon which to forecast performance
- Unable to ensure SOP/regulatory compliance
- Unable to spot bottlenecks and internal processes ripe for optimization

Clinical trials that get off to a good start are more likely to execute well and finish on-time and on-budget. Technology is the critical enabler. With so many multiple aspects to balance across many stakeholders, from finalizing the protocol to coordinating contracts, selecting sites, and recruiting patients, tracking information manually and in a siloed manner simply does not work. The stakes are too high and risks too great to have a decision model based on ad-hoc processes and fragmented information.

Forward-thinking stakeholders looking to improve SSU are reaching out to providers well-versed in the intricacies of SSU, who focus their efforts on it exclusively, and have a proven track record. This emphasis allows for the development of best-in-practice solutions that not only have extensive country-specific workflows as part of the offering, but they also integrate with other eClinical solutions. This allows for ongoing updates to SSU solutions designed to optimize site selection and document completion and management. And overall, this aligns with the regulatory push toward greater use of technology to modernize SSU and the rest of the clinical trial continuum.

It’s not just about speeding up the process; SSU underpins the very foundation of the clinical research value chain. From selecting the right sites from the outset, to operating in a collaborative, transparent fashion with research partners; optimized SSU results in greater compliance, enhanced data integrity and ultimately increased patient safety for participants – progress we can all support.

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