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WHITE PAPER

The Clinical Development Plan

Executing the Clinical Strategy

Introduction

Writing a Clinical Development Plan (CDP) takes time and effort but is ultimately a key part of the navigation system ("the GPS") to bringing an investigational medicinal product (IMP) to market with a compelling patient and payer value proposition. The CDP is the result of translating the vision into a tactical plan with consideration of the potential risks and opportunities that surround the clinical program.

For an early stage pharma/biotech company, the CDP can be extremely valuable and a key indicator of potential success of a program. The CDP is not merely a bulleted list or project plan on clinical studies with timelines and cost. The CDP is made valuable through the multidisciplinary consideration of all components that enable success of the clinical program, leveraging opportunities and mitigating against anticipated risks. This white paper provides tips and best practices on developing and executing a clinical strategy:

- Overview of program-level considerations to support the execution of the CDP and, in particular, how recent updates in regulations such as draft ICH E8 (R1) are changing the IMP development process.

This paper focuses on how to ensure the clinical plan is feasible, focuses on the issues that matter, and mitigates anticipated risk to the program.

Executing the Clinical Strategy

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Feasibility

The concept of conducting a feasibility assessment is a new addition to the draft ICH E8 (R1). Feasibility has traditionally been completed at the protocol level but should be conducted at the program level once the CDP is written (not finalized).

Conducting feasibility at the program level will allow early identification of potential issues related to the planned design of the clinical studies, such as patient selection, selection of comparator, duration, and procedures.

Feasibility at the program level will also allow for planning operational execution of the clinical studies, such as patient recruitment, accrual, country and site selection, as well anticipated timelines and cost. As an example, while enrichment strategies related to patient eligibility may be enhance the treatment effect, it is important to understand the potential impact on patient recruitment.

Clinical teams should begin developing a list of potential countries and clinical sites to begin building relationships, as well as to obtain insights into the prevalence and incidence of the disease or condition, standard of care, unique regulatory requirements, and the past performance of these countries and sites.

In addition, clinical teams should engage with patients and patient advocacy groups to obtain insights on the design and feasibility of the clinical program and clinical studies.

A robust feasibility at the program level will provide a reality check to the optimistic clinical plans and result in more achievable study planning, conduct, timelines, and cost.

Feasibility at the program level will also allow for planning operational execution of the clinical studies:

Patient recruitment

Accrual

Country

Site selection

Timelines

Cost

Patient Recruitment

Patient recruitment continues to be one of the main challenges in the operational execution of a clinical study. Traditionally, patient recruitment was left to the clinical investigator based on their database of patients diagnosed with the disease or condition of interest.

In today's environment, the clinical team must engage patients, patient advocacy groups, and social media experts to develop the strategies to attract, screen, and enroll potential patients into the clinical study. Companies may want to engage with a patient recruitment company to develop a program and protocol-level recruitment strategy.

Further, companies must consider the design of the planned clinical studies and the patient selection criteria as potential barriers to patient recruitment. Studies that are complex, time-intensive, or require invasive procedures will be more challenging to recruit patients. Similarly, overly restrictive eligibility criteria may exclude patients who may otherwise be eligible.

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Quality by Design

Given the recently issued draft ICH E8 (R1) guidelines, Quality by Design (QbD) should be added to the CDP. The QbD section should identify issues or factors that are critical to ensur-ing the protection of study subjects, the generation of reliable and meaningful results, and the management of risk. At the program level, QbD will help identify the critical-to-success factors. As examples:

- An efficacy endpoint reliant on third party interpretation would want to ensure the third party is highly qualified as a critical-to-success factor;
- An efficacy endpoint reliant on imaging would want to define the equipment and process to obtain the image as a critical success factor; or
- A patient's ability to comply with the compliance of the study (e.g. treatment compliance, follow up procedures) may be considered as a critical success factor.

Early stage pharma/biotech companies that have identified the critical-to-success factors across the clinical program are better focused and better positioned to develop strategies to mitigate potential risk.

Risk Management

Once a company has identified the critical-to-success factors, a plan to assess and mitigate the risk can be developed. Risk assessment begins with the describing issues that may occur that would affect the safety of the patients or reliability of interpretation of results. The process includes determining the probability of the issue occurring, whether the issue could be detected, and the severity of consequences if the issue occurred. Once assessed, a strategy can be developed to mitigate the issue from occurring thus reducing or eliminating the risk.

Successful early stage pharma/biotech companies recognize the importance of managing risk as part of the ongoing planning and execution of the clinical program.

Conclusion

Writing a CDP takes time and effort but, in the end, can be extremely valuable and a key indicator of potential success of a program. Download the available CDP template to facilitate the multidisciplinary development of a clinical program that is robust, feasible and aligned with the patient and payer value proposition defined in the TPP.

About the Author

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Margaret McShane is a Clinical Operations professional with more than 30 years of experience across multiple therapeutic areas, including numerous rare diseases. Margaret began her career in big pharma (initially The Upjohn Company; ultimately Pfizer) supporting the execution of clinical development programs and was twice invited to lead corporate redesign efforts to streamline the clinical development process. Margaret has a Bachelor of Science in Chemistry and Biology and a Masters of Business Administration.