Early Phase Case Study

Accelerating development of a first-in-class therapy for sickle cell disease

Overview

A sponsor developing a first-in-class therapy for sickle cell disease (SCD) needed to rapidly generate safety, pharmacokinetic (PK), and early efficacy data to support continued clinical development. The study represented a critical opportunity, as no disease-modifying treatments were widely available at the time, and early signals of efficacy could significantly influence regulatory and development strategy.

To maximize speed and insight, the study was designed as a highly adaptive early phase program integrating single ascending dose (SAD), multiple ascending dose (MAD), and proof-of-concept elements within a single protocol. This approach required careful coordination of healthy volunteers and patients with SCD, alongside real-time data review to inform dose escalation and study progression.



Challenge

This study presented significant scientific and operational complexity:

Adaptive design with evolving data requirements
The protocol required flexibility to allow extension of dosing based on emerging biomarker and safety data, introducing operational and regulatory complexity.

Complex, dual-population enrollment model
The study combined healthy volunteers and SCD patients within a single adaptive framework, requiring distinct recruitment, safety monitoring and operational approaches.

Need for rapid insight to inform development decisions
Early efficacy signals were critical to determining progression into later-phase development, placing pressure on speed and data quality.

Recruitment in a specialized patient population
Enrolling and retaining patients with SCD required targeted engagement strategies and strong site coordination.

Solution

A coordinated early phase strategy was implemented, combining adaptive design, integrated operations and patient-centric recruitment:

- **Adaptive, integrated early phase study design**
  - » Seamless protocol incorporating SAD, MAD, and extended dosing components
  - » Real-time evaluation of safety, PK, and pharmacodynamic (PD) data
  - » Enabled progression from first-in-human through early proof-of-concept within a single framework
  - » Continued flexibility throughout the study to react to the emerging data, including the addition of a Phase II extension
- **Proactive regulatory engagement and alignment**
  - » Early engagement to support acceptance of adaptive design
  - » Rolling review of emerging toxicology and clinical data
  - » Predefined timelines for ongoing safety, PK, and PD reporting
- **Centralized operational model with integrated analytics**
  - » Dosing conducted at a single specialized early phase unit
  - » Onsite biomarker analysis enabled rapid data turnaround
  - » Continuous interim analyses supported fast decision-making
- **Targeted recruitment through a hub-and-spoke model**
  - » Centralized dosing with decentralized patient screening
  - » Collaboration with patient advocacy groups to support enrollment
  - » Patient-centric practices to enhance engagement and retention

Outcome

This integrated approach enabled continuous study progression and accelerated development despite a complex adaptive protocol:

Key results

- No study or patient pauses despite multiple protocol amendments
- Seamless transition from first-in-human into Phase II extension within the same framework
- Dosing duration extended from 28 days to up to 118 days based on emerging data
- Early efficacy signals supported continued development, study expansion and investment decisions
- Accelerated progression from first-in-human to regulatory submission in approximately five years

Impact

The successful execution of this program:

- Enabled earlier, data-driven decision-making
- Supported rapid, accelerated advancement into later-phase clinical development
- Demonstrated feasibility of adaptive designs in rare disease populations
- Delivered high-quality, continuous data to inform regulatory strategy

Summary

This case demonstrates how an integrated early phase strategy — combining adaptive design, proactive regulatory engagement and patient-centric recruitment — can accelerate development of innovative therapies in complex populations.

By enabling seamless progression from first-in-human through early efficacy evaluation, this approach delivered the speed, flexibility and insight required to advance a first-in-class treatment toward regulatory success.

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