Innovative Plan Reopens Sites Three Months Earlier Than Expected After FDA Clinical Hold

Challenges

Syneos Health™ was responsible for the management of six oncology studies with novel immunotherapy treatment. With sites engaged in start-up and active treatment, the client received an FDA notification that the IND applications were placed on clinical hold, restricting screening and treatment of all new and existing subjects. It was critical that the sites were informed immediately.

The clinical hold put the overall study enrollment timelines at risk, and if active subjects discontinued as a result, they would need to be replaced. Syneos Health had to implement an innovative strategy to ensure screening activities and treatment could resume as soon as possible to minimize the impact of the hold.

Solution

The Syneos Health project team had to carefully manage the initial site communication. To ensure the sites were fully and immediately informed, Syneos Health developed the following action plan:

- Email notifications were sent to the site staff with read receipt, and each site was called to confirm receipt.
- Sites were informed that no new subjects could be screened or treated until further notice. Sites were asked to notify active subjects and document the notification in the subjects' records.
- Because all study procedures would continue, with the exception of the study drug administration, sites were reminded to keep data entry up-to-date and to inform the project team of AEs of special interest.
- Sites were told to notify their IRB and any other required committees according to the site's policies and procedures, and Syneos Health notified the Central IRB/IBC on other sites' behalf.

Demonstrated Capabilities

Area

- Hematology & Oncology

Clinical Phase

- Phase I-II

Highlights

With innovative strategies, Syneos Health managed to

- communicate effectively with sites
- keep sites engaged and enthusiastic about trials
- exceed site reactivation expectations by 7.6 weeks on average to minimize impact of clinical hold

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- Site pharmacies were instructed to quarantine the investigational agent until further notice. All drug shipments were placed on hold with the IRT Department.
- Patient-specific and protocol-specific questions were directed to the Syneos Health Medical Monitor.
- Sites were reassured that Syneos Health and the client were working closely with the FDA to address all issues quickly, and that the sites would be notified as additional information became available.

During the Clinical Hold:

- Syneos Health continued to contact sites weekly with available updates and conducted routine monitoring visits to ensure timely data entry, data cleaning and safety reporting. This kept sites informed of trial progress and kept sites engaged.
- Syneos Health spoke with the client weekly regarding priorities, site-specific plans, upcoming IRB submission deadlines and status updates to focus the team toward the same goal at all times.
- For sites not yet activated at the time of the clinical hold, Syneos Health continued working toward activation to the extent possible. Submissions were placed on hold until the new protocol amendment was finalized for sites that had not submitted to the IRB/IBC. Initiation visits to train site staff were conducted at sites that were further along but the site was informed that it would not be activated for screening until the FDA's clinical hold was lifted and the protocol amendment and related documentation were approved by the IRB/IBC.
- Site reactivation timelines were reviewed regularly, and upcoming IRB submission deadlines were used to prioritize sites for reactivation.

Efforts Continued Until the FDA Lifted the Clinical Hold on the IND Applications 10 Weeks Later.

- Following discussions with the FDA and in accordance with its recommendations, Syneos Health worked closely with the client to revise the protocol and study-related documentation.
- A site notification package was prepared and finalized by Syneos Health expeditiously. This package included a cover letter to the sites with the FDA memo lifting the hold, the protocol amendment with the FDA changes implemented, the updated consent template highlighting the language that was non-negotiable per the FDA's approval, additional safety information, updated study-specific manuals and contract/budget amendments for further negotiation.
- To minimize the impact of the clinical hold, sites were reactivated individually for enrollment once the protocol amendment and related study documentation were approved by the IRB/IBC, upon receipt of the protocol signature page and the completion of protocol amendment training.

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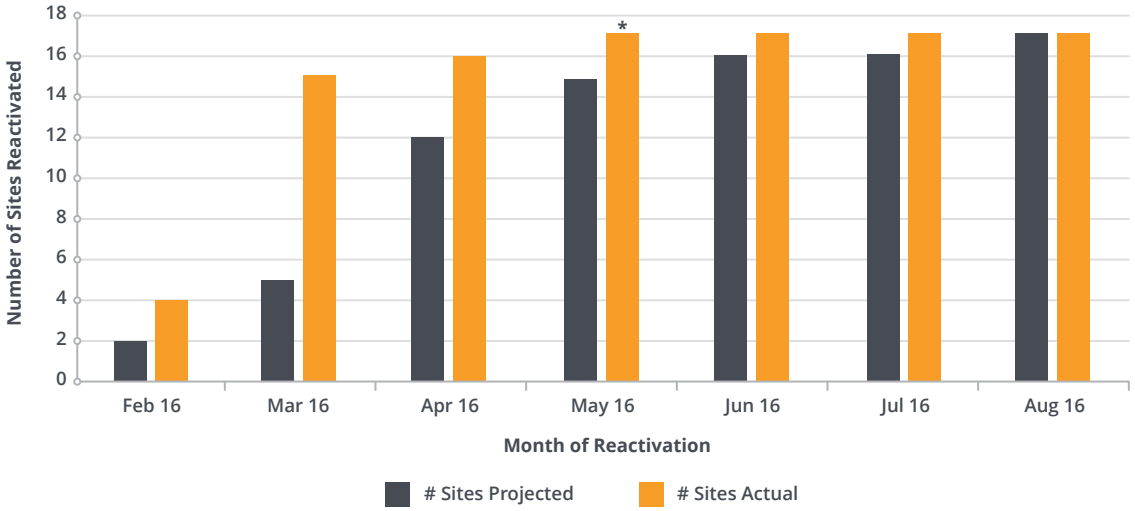
Impact

- Study interest and enthusiasm were maintained across all sites. No sites dropped from study participation, and all sites remained enthusiastic about being reactivated.
- On average, sites were reactivated 8.3 weeks after receipt of the protocol amendment.
- 95% of sites were reactivated on time or ahead of the scheduled timeline to reactivate.
- The Syneos Health action plan lead to the reactivation of sites 7.6 weeks ahead of schedule on average.

Reactivation of Sites—Projected vs Actual



*Indicates that sites were originally projected to reopen in May. Syneos Health was able to reactivate the sites as early as February.

About Syneos Health

Syneos Health™ (Nasdaq:SYNH) is the only fully integrated biopharmaceutical solutions organization. Our company, including a Contract Research Organization (CRO) and Contract Commercial Organization (CCO), is purpose-built to accelerate customer performance to address modern market realities. Created through the merger of two industry leading companies – INC Research and inVentiv Health – we bring together more than 21,000 clinical and commercial minds with the ability to support customers in more than 110 countries. Together we share insights, use the latest technologies and apply advanced business practices to speed our customers' delivery of important therapies to patients. To learn more about how we are shortening the distance from lab to life™ visit SyneosHealth.com.