Dr. Vince Clinical Research

White Paper

Innovation in a First-In-Human Trial

Combating the Opioid Crisis with a Single Ascending Dose (SAD) Study with an Anti-Fentanyl Antibody

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Background

More than 70,000 people die every year from fentanyl overdose, making it the number one cause of death in Americans aged 18-45.[1,2] To combat this crisis, Cessation Therapeutics, a biotechnology company, is developing an anti-fentanyl antibody to reduce the opioid's toxic effects and prevent overdoses. They partnered exclusively with Dr. Vince Clinical Research (DVCR) to run their First-in-Human (FIH) clinical study: a double-blind, placebo-controlled, Single Ascending Dose (SAD) trial. This protocol required the enrollment of 32 healthy volunteers who were dosed in four sequential groups, each separated by a mandatory period of safety monitoring.

"Cessation Therapeutics' anti-fentanyl antibody is a promising and viable lifesaving solution — making the trial's success paramount."

Prior to this trial, Andy Barrett, PhD, the Chief Scientific Officer at Cessation Therapeutics, had worked with many of the DVCR leadership team.

The Challenge

FIH studies are understandably complex, as the investigational product (IP) has never been administered to people before. Therefore, this comes with heightened safety concerns and the potential for unforeseen adverse events. To mitigate these inherent risks, robust study volunteer safety measures must be instituted before study commencement. Furthermore, FIH studies demand fastidious data collection to ensure quality deliverables and minimize the chances for protocol deviations. This particular trial required healthy volunteers who would remain confined at the research site for 14 days and then return to the facility at weekly and bi-weekly intervals for four months — making retention another pressure point. The trial was also operationally challenging because of the 4-hour stability window of the investigational product (IP) from preparation to administration. This, combined with the escalating dose design and an unforeseen need to alter the proposed diluent, required quick and effective management by the DVCR project management and clinical operations teams.

Dr. Vince Clinical Research's Solutions

To help Cessation Therapeutics meet its corporate objectives, DVCR provided full-service support, including access to a specialized team with considerable FIH expertise and streamlined study processes backed by an immense passion for the project.

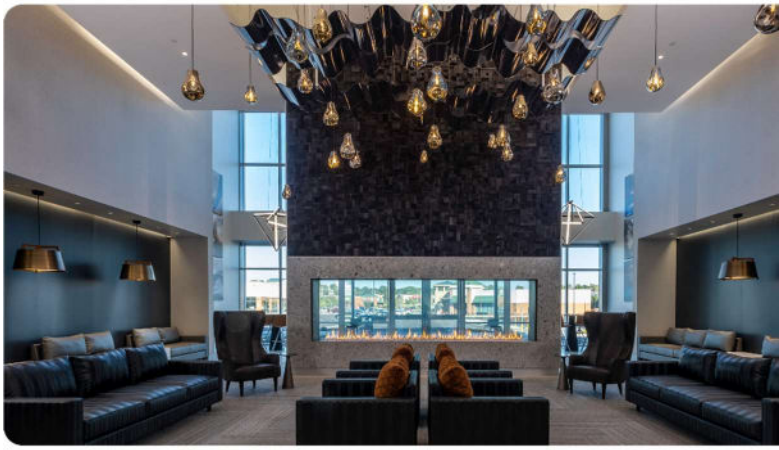
DVCR engaged with the client early to ensure key personnel had the opportunity to review and provide comments on the draft protocol. Working together, they improved the operational feasibility of the protocol, paying particular attention to the schedule of events and the inclusion/exclusion criteria. Additionally, the DVCR team devised a specific, to-the-minute study schedule based on the finalized protocol to minimize deviations and ensure quality data collection. This detailed and comprehensive study schedule was coupled with well-trained clinical research personnel assigned to accomplish every procedural task, from venipuncture to physical examinations to intravenous IP administration. Beyond the clinical staff, DVCR also supplied a seasoned project management team with significant industry experience in early-phase clinical trials. Furthermore, the team provided the client with requested daily updates, closely managed vendor deliverables and communication and kept the trial strictly on

track through keen oversight of sponsor-provided timelines and critical milestones.

The expertise of DVCR was demonstrated by effectively pivoting when the FDA requested that the follow-up period be extended by an additional 60 days for volunteer participation in the study. This two-month addition to the outpatient visits required a significant modification to the recruitment strategy. Upon receipt of the aforementioned change request, the team revised the study plan internally, reviewed all revisions with Cessation Therapeutics and assisted with the subsequent regulatory submission. DVCR had preemptively targeted new clinic admission dates to ensure all involved could proceed immediately following the FDA's second review. DVCR successfully navigated this request all while keeping the client informed in real-time as well as effectively maintaining critical forward momentum with the trial.

DVCR's recruitment and retention expertise was crucial to the success of the trial. The recruitment department conducted a thorough campaign that included social media, television and streaming service advertising as well as direct calls to potential participants from their extensive volunteer database. DVCR ensured that the study budget included sufficient participant compensation and resources to have additional screened subjects on call in case of dropouts or no-shows. Volunteer retention rates were strong secondary to the luxurious amenities offered at DVCR's state-of-the-art clinical pharmacology unit. For the entirety of the volunteers 14 day stay, they had access to a sports-bar-themed dining room, a VIP lounge for quiet recreation as well as a gaming and arcade room.

While recruitment considerations may appear trivial, this is simply not the case. FIH/SAD studies often involve fewer overnight stays and offer less compensation than other Phase 1 trials. This alone can be problematic for meeting the critical recruitment milestones required for dose escalation decisions. If a cohort is short-dosed, it can cause significant downstream delays through the remainder of the study timelines. The additional time needed to recruit, schedule, screen and then dose the remaining volunteers in that cohort could result in a delay ranging from one to four weeks. Furthermore, some volunteers will screen for multiple studies simultaneously with different CROs, reducing the reliability of volunteers to check in for their scheduled group.



FIH/SAD clinical trials can pose various challenges and risks that must be taken into account when considering clinical monitoring oversight and Clinical Research Associate (CRA) assignment. While adaptability, availability and experience are all critical attributes for a CRA, the single most important trait is a strong understanding of the management of complex FIH/SAD early clinical development studies. Experienced CRAs deploy effective clinical monitoring strategies to verify participants safety and collection of high-quality study data. For these studies, CRAs maintain their focus on priority issues such as verifying randomization eligibility of study participants prior to sentinel dosing as well as onsite observation of this initial dosing. The CRAs

verify laboratory sample collection, handling, processing and storage, as well as pharmacy preparation activities within their assigned blinded or unblinded roles. Through the lens of experience, CRAs monitoring FIH/SAD studies can master the agility and flexibility required to adapt to the fast-paced environment and challenges unique to these complex studies.

The pharmacy team established a collaborative relationship with Cessation Therapeutics by providing extensive feedback on the trial design over 12 months prior to when the study commenced. Backed by over 50 years of combined clinical trial experience, DVCR's pharmacy group successfully executed all requirements for this clinical trial. When the client discovered an unexpected need to change the proposed diluent, the DVCR pharmacy team quickly suggested saline as an alternative. Despite COVID-related supply issues, they promptly procured the required saline with help from a specialty vendor.

Another operational challenge was the relatively short window of time in which the IP had to be prepared and administered on the day of dosing. Working closely with the project management team, the pharmacy created a detailed schedule outlining every step of the dose preparation. The schedule included factors ranging from transfer of accountability to study drug administration time as well as storage.

The pharmacy team adeptly managed challenges related to IP administration to accommodate the dose escalation study design. As the individual drug dosage was dictated by volunteer weight, the volume administered differed for each individual participant. The pharmacists outlined steps for calculating the dose escalation in the pharmacy manual and included sponsor review of every dose as an additional safeguard.

The Results

Thanks to DVCR's experience, dedication and responsiveness, the clinical trial was a resounding success despite several potential pitfalls. The study was completed on time and on budget, met all dose escalation milestones as originally planned and fully enrolled all cohorts (plus backups) while maintaining 100% volunteer retention throughout. Most importantly, the team delivered high-quality data to the client on time and as promised. Cessation Therapeutics is now poised to continue advancing this potentially lifesaving medication that could provide a viable alternative to healthcare providers in their battle against the opioid epidemic, specifically with fentanyl.

Enjoy Smarter Faster Data® for Your First-in-Human Study

DVCR is your full-service CRO partner, offering an optimal environment for clinical study execution that delivers high-quality data to advance your biopharmaceutical product.

References

[1] National Institute on Drug Abuse. Drug Overdose Death Rates. 2024 May 14.

[2] Get Smart About Drugs. DEA Administrator on Record Fentanyl Overdose Deaths. Accessed 2024 June 12

About Dr. Vince Clinical Research

Dr. Vince Clinical Research (DVCR) is a full-service contract research organization (CRO) specializing in early phase trials in both healthy normal volunteers and patient populations across a wide range of trial designs and therapeutic areas such as neuroscience, substance abuse, pain, cardiometabolic disorders, infectious diseases and many others. CRO services include project management, data management, biostatistics, statistical programming, PK/PD analysis, medical writing, monitoring as well as site feasibility and management for multi-site trials. Additionally, DVCR operates one of the most innovative and technologically advanced clinical pharmacology units in the world with over 90 beds for overnight confinement, a cGMP compliant pharmacy as well as luxurious amenities to support diverse study participant recruitment and retention. By leveraging technology and one of the country's most experienced leadership teams in early clinical development, DVCR provides Smarter Faster Data® to their biopharmaceutical clients.

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