MEDSOURCE
Taking Relationships as Seriously as Science

CASE STUDY

Idea to Market – delivering clinical trial success in record time

The pathway for developing new medications and moving from idea to preclinical development tests, complicated clinical trials, and regulatory approval by the FDA is often an expensive and long road. In fact, industry research notes this process can take several years – usually 10 to 15 – and hundreds of millions of dollars. For an organization needing to move a drug quickly to market or struggling to overcome the hurdles that can arise during a clinical trial, it can seem like an uphill battle to the finish line.

With both time and money at stake, organizations need a clinical research organization (CRO) partner that has a proven record of successfully operating under significant time constraints, while still delivering a high-quality and successful clinical trial, moving an agent from proof of concept (POC) through to New Drug Application (NDA) status quickly and efficiently.

THE CHALLENGE

POC to registration in three years

MedSource was selected by a clinical-stage biopharmaceutical company to deliver a small POC study, that included only six subjects. The POC study was terminated early due to positive results, and MedSource was then tasked to execute a phase IIb study with the same compound. During the phase IIb study, the interim findings were presented to the FDA, which resulted in the expansion of the trial to include additional participants. Soon thereafter, the study was fast-tracked by the FDA, and MedSource was tasked with executing two phase III trials of an intravenous neurosteroid in the treatment of moderate and severe postpartum depression (PPD).

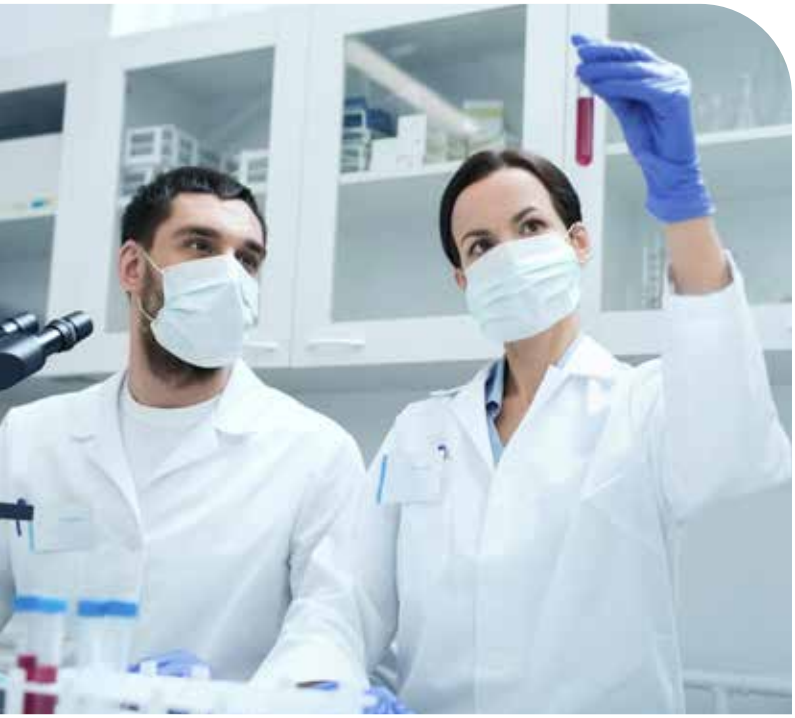
At the start of this project, MedSource encountered numerous challenges that had to be resolved for each step of the process to be a success. Notable hurdles included securing enough patients that fit the criteria and the lack of an established standard of care for patients with PPD (other than traditional antidepressants and talk therapy, which can take weeks or months to show any effect).

One complication, while positive for the program, but unknown at the outset, was the sequence of events that would lead to the FDA requesting that the phase II trial be abandoned before it was completed and the trial move directly to a phase III NDA study, effective immediately.

While certainly a rare occurrence, it is a scenario that many organizations would welcome, if not strive for. From a delivery standpoint, however, many organizations would be hard-pressed to find a CRO that could drop everything and move at a significantly increased pace, while still producing a successful, quality trial within the new, accelerated timeframe.

In the space of three years, the program moved from POC to a phase II trial, and then to a phase III trial registrational study. Given this escalation from a small study to a high-profile, larger study, MedSource had to adapt quickly, a feat made even more difficult by the fact that this was the first phase III program conducted specifically for women with PPD. This required an almost immediate reshuffling of resources internally to ensure the trial would have all of the needed elements in place. In addition, a more aggressive program was needed to source a significantly larger patient population – 120 subjects for part B for testing severe PPD and 104 subjects for part C for testing moderate PPD – a task MedSource had already identified as a challenge.

Affecting approximately 10 to 20 percent of mothers giving birth in the U.S., PPD is a mental health illness that affects women either in the third trimester of pregnancy or within four weeks of giving birth and can last for months after giving birth. The number of women impacted by this disease may in fact be significantly higher, but due to the stigma attached to this illness, many cases go undiagnosed or unreported. Symptoms include feelings of sadness, loneliness, worthlessness, restlessness and anxiety lasting much longer than a few weeks.



There are no approved treatments for PPD, and currently, patients exhibiting symptoms are commonly prescribed antidepressants. The timing for when women interact with their clinicians exacerbates the difficulties of identifying and diagnosing PPD. For example, the first checkup for a baby is about six weeks after birth, and not all states have a formal assessment of the mother at this time. In addition, the stigma attached to PPD and the reluctance of mothers to come forward to admit to their symptoms added to the challenge MedSource had to work through in order to secure subjects to participate in a trial of this nature.

THE STRATEGY

Awareness campaign to secure trial subjects

To combat the stigma attached to PPD and the lack of education about the illness among new mothers, an awareness campaign through targeted advertising was deployed. The campaign also encouraged new mothers who were struggling with depression to seek help and consider being a part of the clinical trial. As PPD also impacts husbands/fathers and other family members, the campaign additionally targeted these groups to raise awareness of the symptoms of PPD and communicated the need for their loved ones to seek help. Working with community groups, social workers, churches and other facilities that already had established PPD educational programs was another avenue that assisted MedSource in identifying subjects who fit the criteria of the trial.

The approach was successful, and MedSource was able to secure all 220 subjects in a matter of seven months, a very quick turnaround, especially given the challenges that had to be overcome. As an example of how fast the team mobilized, the first patient was secured and screened the day after enrollment opened, demonstrating not only MedSource's ability to deliver results, but that its proven approach and flexibility can overcome the many hurdles routinely faced throughout a trial. In the case of this PPD trial, it was working under significant time constraints together with the complications and sensitivities around engaging this particular patient group.

Resourcing the trial quickly and effectively

Due to accelerated pace of this trial, it was critical for MedSource to be able to mobilize quickly and effectively, adapting to each and every changing circumstance along the way. Unlike larger CROs, MedSource can operate more nimbly and with a greater degree of flexibility. In the case of the PPD trial, the team was able to ensure appropriate resources were assigned and staff could hit the ground running by changing team structures, especially once the phase III trial was fast-tracked. Up to eight CRAs were on-boarded almost immediately. Given MedSource's previous experience with the neurosteroid from a different trial, the team was already familiar with the agent, necessitating less time to get up to speed.

Continuity of staff throughout the entirety of a trial is often unheard of; however, during this PPD trial, the same team was involved from the POC stage through the end of the phase III trial. MedSource has a philosophy that strong relationships with clients lead to strong results, and part of that commitment is putting in place a team that is 100 percent dedicated to the organization and its trial.

Managing the trial sites

Because the subject had to be an inpatient for 72 hours and receive an IV fusion for 60 hours straight, the trial was onerous on study participants. Consideration had to be given to where the patient's child would be during this time, and compensation was provided for a caregiver to tend to a newborn at the facility if no other arrangement could be made. Additionally, patients could not breastfeed for the first 12 days after initiating the intravenous agent treatment, but were then free to continue doing so without any issue. With these numerous factors, MedSource worked with the sites to be sure that all of this information was properly communicated to the patients, including that patients were educated on any concerns (particularly around breastfeeding) and that the process of how the drug would be administered was explained accurately.

Regular communication with site staff was a critical component of this trial, and a dedicated CRA was assigned as the point person for each site and available either via phone or in person when required; bi-weekly meetings were also scheduled to discuss any issues that might have arisen. In addition, the trial manually randomized subjects. Within 24 hours of a patient arriving at a site, treatment needed to start. The dedicated CRA had to be available to answer a call at any moment to ensure he or she could assist in securing the subject and that treatment wasn't delayed.

Being readily available for not only the sites, but also the client, at any time of the day or night demonstrates how MedSource becomes an extension of the organization it is working for, operating as a partner and ensuring a seamless and transparent relationship to deliver the best results and a high-quality trial.

Regular data reviews

The client regularly required data pulls, every 20 subjects, which is more frequent than a normal phase III trial.

MedSource CRAs had to be on-site within two days of the 20th subject to conduct interim database locks, review data, and send top-line results to the client within three to four days.

Reliability of the data was critical. Decisions had to made about the progress of the trial quickly and effectively, especially given the speed at which the trial was being operated. During the entirety of the trial, MedSource was never delayed in delivering relevant and reliable clean data for analysis.

THE OUTCOME

MedSource was successful in securing more than 220 patients and delivering a quality clinical trial with positive results in less than three years, adapting to the changing environment throughout this time that included the fast-tracking process from the FDA.

The success of this trial can be attributed in part to MedSource's ability to anticipate what the client wanted or might need, before being asked, something only a true partner can do. The team's dedication and availability at all hours of the trial – both to the site staff as well as to the client – ensured quick responses, which resulted in not only securing enough subjects, but also delivering the regular datasets needed to make decisions about the trial's progress.

Overall, the trial was lauded as a huge success, with the agent providing patients with a rapid and durable reduction in depressive symptoms over 30 days in both placebo-controlled multicenter trials. This was also a step forward in the development of treatments for PPD and helped to alleviate some of the stigma attached to the illness.

Pending final FDA approval, the new drug is scheduled to be released to the market in 2019.

VISUAL SNAPSHOT

- **Clinical trial:** Two separate phase III trials in the treatment of moderate and severe postpartum depression (PPD)
- **Condition:** Moderate and severe PPD
- **Purpose:** To evaluate the efficacy and safety of intravenous agent in patients with PPD and deliver improvements on the Hamilton Rating Scale for Depression
- **Patient-type:** Mothers aged 18 to 45 who had given birth within six months of the trial, showing symptoms of moderate or severe depression that began no earlier than the third trimester and no later than the first four weeks following delivery, and located in the U.S.