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Lilly's Effective New Strategy TO CUT CLINICAL TRIAL TIMELINES

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A clinical trial transformation is currently underway at Eli Lilly & Company. Two years ago, it was taking the company an average of 10.5 years to go from first patient dosed to actual product launch. The time it took to simply enroll patients in trials was averaging four years. That means 40 percent of the time a drug was in development was spent simply recruiting patients. There is a set amount of time that is spent treating patients and analyzing data. Oftentimes that cannot be changed. But enrollment was one area where the company felt improvements could be made.

"The situation had to change," says Anne White, Lilly's VP of next generation development and project management. "We knew we had to find a way to get our medicines to patients faster." CEO at the time, John Lechleiter, told his leadership team, "I want to change this dynamic. We need to be fast along with having a great portfolio. How do we make that happen?" According to White, for the past two years the company has worked toward turning his vision into reality.

When White was still serving as VP of oncology at Lilly, the time it took to get new drugs to market was a concern she would often hear from patients. When a product was nearing the finish line, those patients would want to know when they could get access to it.

"When a patient is ill and in need of a drug, it's very difficult to tell them they have to wait a few more months," laments White. "We would receive many of those calls, and talking to patients and caregivers was always very difficult. We knew that getting a drug to market just three or six months sooner could make a huge difference in the lives of a lot of patients. In some cases, it could actually save lives."

A PASSION FOR PATIENTS

White notes there were many nights when she could not stop thinking about those patients. That, along with Lechleiter's vision of a faster trial process, motivated and convinced her to take the newly created position in next generation development. "I came into the job with a lot of passion," she says. "The passion came from an understanding that medicines cannot do any good until they are in the hands of patients. When I made the decision to jump into this role, it was very personal to me."

The first thing Lilly did was put together a small team to focus on the key factors — one of which was enrollment — that would help trials progress faster. "Some of the changes we made can be instituted at any pharma company," says White. "They will certainly raise Lilly's boat, but I think they also will raise all boats. Our primary goal was to get drugs to patients faster, and that does not entail just our own drugs. Making patients more aware of clinical trials as a treatment option and eliminating many of the myths will help all companies better recruit for trials."

When it comes to enrollment, White felt there were three things that had to be done. First, patients needed to be aware of what trials existed for their disease in their location. Second, they needed to be able to enroll in trials that they located. Finally, once enrolled in a trial, they needed to stick with the study until the end. Lilly's plan for transforming the patient recruitment process tackled each one of these issues.

MAKE PATIENTS AWARE

The first thing White felt she had to do was make patients aware of trials that were underway at Lilly. She knew that most physicians do not discuss clinical trials with their patients, and websites like ClinicalTrials.gov are difficult for patients to navigate. Some companies publish lists of trials they are conducting, but White felt a different approach was necessary.

For many patients, the whole idea of participating in a clinical trial is a mystery. Therefore, the company created a website called *Lilly Trial Guide*. Patients could go to the site and get information on trials and how to participate in them.

"We had to somehow demystify clinical trials," says White. "There is a lot of misinformation that exists. Patients think they will not get treated as well in a clinical trial as they do when visiting their physician. (Research shows the frequency and quality of care is actually higher in a clinical trial.) They also believe they will not get access to good medicines. For example, one myth is that some cancer patients participating in a trial will be treated with a placebo. In most cancer trials that is simply not true. There were even patients who felt they would be treated with something that was untested and unsafe. We knew we would have to change those false perceptions, since they deter patients from participating."

On *Lilly Trial Guide*, prospective trial participants can watch a documentary about patients who have been in a trial. The patients discuss what actually happened to them in an attempt to bust many of the myths that exist.

Navigating the site is fairly simple. Users simply select their condition from a drop-down menu, enter their zip code, and the site produces a list of trials. If no studies match their condition or location, patients can opt to sign up for email alerts if a study becomes available. If trials are available, a map shows the study locations and details such as study title and status. An outreach campaign on Twitter (titled *A Hero's Journey*) features the stories of patients who have participated in trials. The tweets contained links to bring perspective patients to the Trial Guide website.

Thus far Lilly has found that users are spending an average of eight minutes on the site – exploring information and watching videos – before they even attempt to search for a trial. Patients from 90 countries have accessed the site, and between 15 percent and 20 percent of them go so far as to request additional information on a compatible trial.

ADDRESSING PATIENT ACCESS

Once patients are aware of available trials, getting them to participate can still be difficult. In talking to patients, White learned that many of them felt participating in a trial would be a difficult regimen to commit to. Others were unsure of whether they would qualify for one.

With *Lilly Trial Guide*, a patient can request additional information on a trial. That request will take them to a separate, institutional review board-approved microsite that contains additional trial and contact information. The site also contains inclusion and exclusion criteria. Patients can even request to have someone call or email them with more information or to answer questions.

"The inclusion/exclusion criteria are important because patients can learn whether they qualify for a trial before beginning the process of requesting inclusion in it," says White. "The information is also presented in layman's terms, rather than the technical language found on ClinicalTrials.gov. Patients are asked questions such as other treatments they have taken. If they meet the trial criteria, they may opt to have someone contact them. This prescreening also keeps the site from being overwhelmed with queries from patients who are not eligible for a study."

While White would not say exactly how many patients have enrolled in trials via the site, she does note that trials are enrolling faster and the effort is definitely paying off. The Twitter campaign alone has resulted in thousands of tweets that have driven interested patients to the website.

"This effort has been far more effective than blasting something out on Facebook or pumping more money into an ad campaign," says White. "Our focus is on getting patients onto the Trial Guide website and letting them find their way to a trial. This has reaped far greater rewards than spending millions on advertising to the general population and hoping you get through to a potential patient. The industry needs to be more proactive. We can't create a website and just hope patients will discover it. To be successful, you have to have new, interesting, and valuable content that people find helpful and will want to share on social media. That is what will keep them coming back."

ENGAGE ADVOCACY GROUPS

Another cog in the effort to provide patients with access to trials is developing good relationships with advocacy groups. Advocacy groups representing patients with migraines, Alzheimer's, and cancer are currently a primary focus for Lilly.

Advocacy groups have their own websites and publish their own social media content. If they find a trial they believe will benefit patients, they are apt to recommend it. Lilly has been active in working with these groups and soliciting feedback on trial designs. White believes that involvement makes them feel more comfortable recommending trials to patients.

"That has definitely played a part in the success of our enrollment effort," says White. "Most recently we have seen success in the areas of Alzheimer's and migraines. We have found those patients to be very active on the internet and taking part in advocacy groups. These groups are a trusted source for them, and they will go to those sources for advice on trial options."

Minorities continue to be disproportionately underrepresented in trials, and patient groups can be a good source for recruiting those individuals. Some of the myths White mentioned earlier are even more prevalent in minority populations. Advocacy groups are a good way to help patients overcome their concerns. A patient's treating physician is almost always a trusted source of information, and Lilly is also reaching out to, and expanding, its investigator network in areas with high minority populations. The goal is to train these physicians and investigators on clinical trials and how to best present them to patients. As a result of this effort, Lilly also has seen its minority participation rates increase.

Finally, proper screening is important to getting the right patients into trials. Up until now, White notes screening has been a manual process for pharma. Lilly believed it was screening 10 patients for every one that was enrolled. Once the company started tracking the data, it found it was actually screening 20 patients for every one that was enrolled. Failure to monitor that correctly can greatly throw off a company's screening timeline.

In order to get a better handle on this, Lilly has moved to a cloud-based system where sites can enter the prescreening information. This allows Lilly personnel to more quickly analyze the information and determine whether a large number of patients is getting screened out. If that situation occurs, the company can take another look at its inclusion/exclusion criteria to see if there is a problem.

"We had a pediatric diabetes study where some patients were being omitted from the study because they had not been on their prior treatment long enough," says White. "With this new cloud-based system, we were able to continue tracking them. That allowed us to go back to them once they had been on the treatment long enough to see if they were still interested in participating in the trial. In the past, these patients would have been lost since we did not have a way to digitally track them."

Sometimes new tools create more work for trial sites, and personnel find them difficult to use. In this case, site staff found the cloud-based system easier to use than filling out sheets of paper. White notes one study where some sites used the new tracking tool and others did not. The sites that did use it ended up with 23 percent more patients participating in the study than those that did not. It also helped Lilly to determine, in real time, whether they needed to open additional or fewer sites.

THE PATIENT VOICE INCREASES RETENTION

Getting patients recruited into a trial is a challenge, but getting some of them to stay engaged is equally difficult. Patients dropping out can delay a trial or cause it to be cancelled. To address the retention problem, Lilly created a new program called CoLAB. The program brings together the clinical research team with patients, nurses, and physicians to perform what could best be described as a dress rehearsal prior to the trial protocol being finalized.

"If pharma wants to increase trial retention rates, it cannot design protocols without considering the voice of patients and sites," claims White. "Patients often drop out of studies when the trials are too long and intensive. Many do not have the time or stamina to do all that we ask. If we can determine ahead of time what is and isn't acceptable, we can cut the dropout rate. CoLAB is helping us to do exactly that."

With CoLAB, Lilly researchers, study coordinators, doctors, nurses, and patients meet face-to-face to walk through the trial protocol. During the day-long simulation, everyone involved will share their thoughts and ideas on trial elements such as planned medication dosing, study visits, and required samples. The feedback is invaluable.

"We once had a protocol that proposed central electrocardiograms for the study," says White. "Feedback we received noted that would not be feasible for many sites in Europe. As a result, we were able to adjust the protocol. Another example is a migraine trial where patients told us the time frame we had set for completing diary entries was not possible. These situations could have resulted in protocol violations and patient dropouts. Instead, the issues were fixed before the trial even started."

White is aware of many patients who indicated they would not have chosen to participate in a trial had the original protocol been in place. In fact, almost every CoLAB session has resulted in changes that made the trial more attractive and hospitable for patients. Site administration also likes CoLAB and have stated they finally feel they have a voice in the protocol-design process.

SIMPLIFIED CONSENT FORMS

One additional factor impacting retention is improved and simpler consent forms. "Simplified consent forms don't just demystify the trial," states White. "They actually have a profound impact on retention. If patients do not understand what they are consenting to, it is easy for them to later say the trial is not what they signed up for. If that situation arises, you lose the patient. A simplified consent form can prevent that situation. If patients understand what they are consenting to, they will be more willing to stick with it. No one wants to be surprised by the requirements."

A 15-page consent form with technical language will always leave patients confused about what they will be asked to do. Electronic informed consent forms with simple language are something Lilly is piloting. For patients who want to learn more, videos are also available to clearly explain trial protocols and procedures.

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Finally, there are patients who opt to not participate in trials (or back out of them) because of required travel to clinics. For them, Lilly has begun using a tele-health solution. This allows patients to be seen by a physician and receive treatment over Skype. Research has shown that approximately 15 percent of patients opt to not participate in trials simply because of geography. Telehealth allows Lilly to access patients in places where there may not be a clinical site. Drugs are shipped directly to patients who will then get tests like ECGs performed locally.

Thus far, Lilly has seen its efforts paying off. The company has already cut a full year off the start-up process, reducing it from four years to just three. But the area of patient recruitment is still rife with more opportunities. The company's goal is to reduce the time by another full year.

"If we achieve that goal, we will have cut the enrollment time in half from where it was two years ago," says White. "Combined with other changes we have made, we have already been able to take our total development time down from 10.5 years to just 8.5. We are in some fairly intense, high-need disease states, and many of them take more time. We are particularly proud of the 8.5 number simply because of the challenging diseases we are involved in."