by Denise Myshko

Patient-Focused Drug Development

Biopharma companies and regulators are working to put the patient truly at the center of drug research and development.

Empowered patients are redefining the healthcare environment on their own terms. Today, patients and advocates are playing a more central and proactive role in managing their own healthcare. This shift is reshaping traditional models of drug development to consider the patients' needs in every step of the clinical trial design process.

Additionally, increased competition within the drug development landscape has resulted in an overabundance of clinical trials seeking too few participating patients. While an increase in patient-focused development won't alleviate all of the challenges in drug development, it certainly improves the patient participation aspect of the equation.

Involving patients early in the protocol process allows pharma companies the opportunity to receive feedback on their proposed procedures and examine areas of improving trial participation. This pre-development work can help round out and provide insight into areas that resonate most importantly with patients, which allows for a more attractive protocol and more focused presentation of the clinical trial offering to prospective patients.

Ultimately, these interactions provide notable reminders to pharma teams that their research is focused on people. This exposure creates additional opportunities for pharma team members to examine ways of reducing patient burden — for example, fewer procedures or less onsite office time — as a standard approach to their development process.

There was a time when it was unheard of for patient advocates to be part of the scientific discussions and decision-making process when designing a clinical study or defining a drug development strategy, says Gissoo DeCotiis, senior director, patient advocacy, Daiichi Sankyo. "For most of history, patients have not been provided with the opportunity to take an active role in the clinical design and implementation process."

Today, biopharma companies are actively working to put the patient truly at the center of drug research and development.

Ms. DeCotiis says patient and patient advocate perspectives can provide a first-hand look into the challenges people living with a certain disease or condition face daily. The advent of patient-focused drug development has underscored the priority of engaging the voice of the patient in therapy development. "Learning patients' perspectives ensures that the reality of the their needs and concerns are considered when a study is designed and executed to enhance the feasibility of the clinical trial," she says. "This approach also allows researchers to proactively inform, educate, and explain the requirements of the studies and overarching needs of the research program in language and approaches relevant for patients."

Companies in the industry, including Daiichi Sankyo and others, have begun to understand the importance of identifying best practices from other industries that routinely consult with their end consumers from the earliest stages of their product development.

Ms. DeCotiis, who spent her early career at American Express, was specifically brought into Daiichi Sankyo to further build patients' insights into the fabric of the organization. "True change requires having strong and influential champions for patient engagement within organizations," she says.

> Companies are implementing detailed, patient-focused protocols so that patient engagement is viewed as a long-term investment with sufficient and sustained resources to reproduce outcomes.
>
> **GISSOO DECOTIIS**
> Daiichi Sankyo

Incorporating the patient's voice into the drug development process ensures that the therapy being developed is ultimately better designed to meet the needs of the patient, taking into account treatment benefit, treatment burden, and patient preferences, says Patrik De Haes, M.D., CEO of Oxurion.

"This ultimately improves the clinical trial process as patients will be more likely to seek out an investigational therapy that captures their voice and takes into consideration their needs," he says. "Further, incorporating the patient's voice into the design of a clinical trial can create a more engaging and positive patient experience with the potential to ease recruitment and increase retention, which ultimately ensures data integrity."

Comprehending the burden a clinical trial can have on a patient's life can increase the company's awareness and how to most accurately capture patient outcomes, Dr. De Haes says.

Patient-focused drug development is a step in the right direction, but pharma can go beyond building a better drug and demonstrating its clinical efficacy, says Patty Zipfel, VP, scientific strategy, MicroMass Communications. "So far, the movement has prioritized collecting data from trial participants to identify meaningful clinical endpoints. However, with the right approach, data gathering can paint a much broader picture of the patient's overall treatment experience."

To understand the factors that may ultimately impact treatment success, she says companies need to look beyond the clinical efficacy endpoint and conduct true patient-centered research. "This means taking the opportunity to get a complete picture of the patient experience: how patients learn about, cope with, and manage their conditions on a day-to-day basis. Listening to patients before, during, and after clinical trials can help identify gaps in critical elements needed for patients to live better with their conditions and ultimately improve their success on treatment."

Once the entire patient experience is understood, pharma companies can then follow through by creating a patient-focused drug experience.

"A patient-focused drug experience will then help fully realize the potential of patient-centered care by addressing all aspects of condition management, including successful incorporation of a new drug into their lives," Ms. Zipfel says. "Pharma companies can also reach patients with more meaningful messages, resulting in increased engagement. Prelaunch marketing helps patients better manage their condition and understand themselves and their role as patients. Launch marketing becomes more practical and helps patients incorporate the drug into their lives. And it all dovetails into improved adherence."

While many in pharma speak of "patient centricity," the industry has been slow to design programs to adequately support and provide human-to-human interaction, for example, deploying individuals such as nurse educators who can guide patients from enrollment and informed consent all the way through to the end of the trial, says Karen Josey, VP, business development, VMS BioMarketing.

"Some new roles and new tactics have emerged within pharmaceutical companies and CROs — for example, patient liaisons, direct-to-patient (DTP) teams, patient Web portals — but our industry still has a long way to go toward giving patients the full measure of support they need while participating in a clinical trial," she says.

Some new roles and new tactics have emerged within pharmaceutical companies and CROs — for example, patient liaisons, direct-to-patient (DTP) teams, patient Web portals — but our industry still has a long way to go toward giving patients the full measure of support they need while participating in a clinical trial.

KAREN JOSEY
VMS BioMarketing

Patients' Voices

BARBY INGLE
President, International Pain Foundation, Complex Regional Pain Syndrome

The clinical trial process could be improved with more transparency. As a patient who participates in a clinical trial, I would help the trial staff by playing an active role in their process from the patient's perspective. At the same time, the sponsor is gaining access to important research treatment information and how patients are affected by such factors as time, location, and ways to participate meaningfully despite disabilities, before the trial is open to participants. Best of all, I would be helping others with the same disease by contributing to both current and future medical research.

Giving patient input for a clinical trial prior to the trial beginning to collect data on the subjects can benefit the disease community because it helps add to scientific knowledge. People who take part in trials are vital to the progression of treatment. It's importatn to remember that participating in clinical trials is not right for everyone. Having the opportunity to be the first to benefit from a new method being tried can be rewarding and scary at the same time. It is a risk for the patients who go first. Having patients help design the process can make it easier and less extensive for the patients in the trial.

BARBARA JACOBY
CEO, Founder, Let Life Happen
Breast cancer
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With the addition of electronic medical records, oncologists do not have as much time or, in many cases, the inclination to help their patients in this arena. I am hearing more and more that patients are being dismissed with the message from their oncologists; "There is nothing else that I can do." The process needs to have a better central matching program available for patients to participate and for some of restrictions being lifted for patients who are dealing with other health problems in order to reach a wider patient pool on all levels.

Most often, it is distance and travel for patients to get to the location of the trial and the cost to the patient in terms of being away from home, work, etc.

A survey last year by SCORR Marketing found that patient engagement is a low priority in clinical trials. While patient engagement has been a hot topic across the industry for some time, actual investment in patient engagement initiatives was found to be weak, at best.

Despite growing evidence of the benefits of doing so, more than one-third (41%) of the respondents' companies did not solicit feedback from patients at all. Of the companies that did integrate patient perspectives, most used surveys, followed by patient communities and patient advocacy groups; 13% indicated that they used other methods. However, when respondents were asked to prioritize their companies' long-term goals for patient engagement initiatives, half responded that they wanted to determine which outcomes were important to patients, 41% hoped to increase patients' potential inclusion in future studies, and a third responded that they anticipated their outreach would encourage patients to be clinical trial advocates in the future.

Being Patient Focused Improves Outcomes

Patient input into drug development is not intended to replace the scientific and medical knowledge and rigor. Rather, the patient perspective is a way to enhance and improve the drug development process, particularly serving as a reminder that patients have lives ongoing outside of the protocol in which they're volunteering their participation.

"Patient input should be a qualifying lens for pharma team members to examine areas to streamline or reduce the burden of the procedures included within the protocol — and the manner and frequency collected — to provide data to the protocol and hypothesis," says Michael Keens, chief operating officer, Firma Clinical Research.

The patient perspective encompasses both ensuring the most efficient and focused means associated with the schedule of events, as well as reviewing how the use of ongoing advancements in areas such as wearable technology and modernized healthcare through decentralized/home visits can be incorporated to collect the same data in a less intrusive manner to the patient. Similar to reviewing and accounting for previous research or competitors in the

Balancing Hope and Risk: The Motivations and Barriers to Patient Participation in Clinical Trials


H. Watson Eccard

The 21st Century Cures Act's guidance for Patient-Focused Drug Development calls for incorporating the patient voice and experience in development of new treatments. Nowhere is this more vital than informing clinical trials, where the expertise of current patients can not only increase recruitment and retention rates, but better the experience of those who will eventually participate in the trial. Inspire recently researched caregivers' and patients' attitudes and perspectives toward clinical trials, and found that most patients and caregivers want to contribute to the development of new treatments. In this research, more than 1,600 Inspire community members, representing such diseases as ovarian cancer, prostate cancer, psoriasis, and scleroderma, took an online survey. Nearly all the respondents were patients, and more than half of the respondents were 60 or older. Of those surveyed, 96% showed interest in learning about clinical trials and 95% showed at least some interest in participating, but only 15% had participated in clinical trials.

Patients have an overall positive outlook around clinical trials and see them as essential to developing new treatments and being critical to increasing medical knowledge. Patients understand the importance of clinical trials — 92% agree that clinical trials are essential — and many patients see clinical trials as a source of hope. In addition, clinical trials are seen as producing new and better treatments and adding to medical knowledge about conditions, including identifying underlying causes of the condition and developing early detection methods.

Patients are also motivated by altruism. Many patients say they want to help others with their condition, and they see clinical trials as a way to do that. Even patients whose condition was well-managed or cured may be interested in clinical research to help the next patient.

So, then, what is holding patients back from participation? For a significant subset of patients, their perception of clinical trials positions them as "risky" and "a last resort option."

More than a third agree with the statement, "Clinical trials are risky," and 42% said they worry about the safety of the patient in a clinical trial. From a patient or caregiver perspective, the biggest concern about participating in a clinical trial is side effects; 83% said information about side effects is very important information to have when deciding whether to participate in a trial, with many fearing side effects would cause long-term or permanent damage. At the same time, a quarter of the respondents said they would only participate in a clinical trial if they knew they would not get a placebo.

Patients are interested in learning more about clinical trials, but access to information and to clinical trials can be a barrier. Of those that have independently researched clinical trials, 28% said they had trouble finding information. One in five respondents said that clinical trial information is too confusing. When patients are considering a clinical trial, they want as much information as possible. Top areas of interest include eligibility information, required tests, phase of the trial, known side effects or drug interactions, and background information on the experimental treatment — if it's a new drug or a new indication for a previously approved drug.

Trial logistics are also important to patients. Logistics don't motivate a patient to join a trial, but it will make patients stay away. Cost is another concern for many participants.

Patient expertise is the key to lessening the gap between the 95% who are interested and the 15% who participate in a trial. The industry can turn to patients to inform trial design, identify information that is most relevant and important to potential trial participants, and overcome some of the logistical and other challenges associated with clinical trials. Patient-focused methods in drug development are gaining ground in overcoming many of these challenges. An approach that directly involves the patient's voice in design allows the intersection of the physicians who are experts in the treating illness and patients who are experts in living with it, helping the former to understand what is of value to the latter and improve the recruitment, retention, and experience of trials overall.

Editor's Note: Hannah Watson Eccard is a Research Manager at Inspire.

With patients contributing to patient experience data, patient perspective information, and other real-world evidence, clinical trials and the ensuing therapies are substantially more patient-centric.

PAUL MELMEYER
NORD

development field, pharma companies and their protocol teams benefit when integrating the patient perspective into their processes by ensuring only the necessary data are collected and by creating a protocol in which patients will support by participating.

"The more pharma companies integrate these perspectives into their development programs, and not merely as a box check, as one patient advocacy head noted at an international conference, the more successful the development landscape will be for study teams and patients," Mr. Keens says.

A patient-centered drug development approach leads to greater engagement in clinical trials, says Alkahest CEO Karoly Nikolich. "Patients are more comfortable in the trial if they believe their voices are actively being heard and that they appreciated as a vital part of the overall process. If patients believe the trial meets their needs, they'll engage with their community and recommend fellow patients to screening centers. This leads to better recruitment, adherence, and fewer drop outs. Ultimately, patients are more informed and more empowered to make an educated decision about their care."

Many pharma companies receive input from patient representatives highlighting real-world examples of their experience, which is a good first start to being patient-focused.

"Some pharma companies limit the involvement of these patient representatives to merely providing a first-hand account of their struggle or challenges with their disease/disorder, while others fully embrace this relationship to include having patients provide

Incorporating the patient's voice into the drug development process ensures that the therapy being developed is ultimately better designed to meet the needs of the patient.

DR. PATRIK DE HAES
Oxurion

direct input on their proposed protocols," Mr. Keens says.

"For example, one pharma company received patient feedback requesting increasing the font size of the study detail to facilitate their review prior to volunteering," he says. "Another trial had a patient forum request additional support and directions for caregivers who were supporting the patient in the trial. This type of direct patient feedback may seem small but it makes a significant difference to those participating in clinical trials."

He says a more advanced approach several pharma companies have undertaken recently to increase their patient focus is viewing protocol design as a holistic process driven by the creation of a "protocol/development design" group.

"Such groups are composed of cross-functional team members from within the pharma company and have the goal of designing a protocol to be as minimally intrusive as possible to the patient while more efficiently advancing drug research," he says. "It's not just about good inter-company communication, most often the teams strive for and achieve a protocol with fewer study procedures for the patient to undergo, or include remote visits to reduce the number of times patients need to visit investigative sites."

Patients' Voices

EFFIE KOLIOPOULOS
Writer, Blogger, Vlogger and Patient Advocate
WEGO Health, Arthritis Foundation
Rheumatoid arthritis, juvenile arthritis, disability
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Companies need to make sure patients and their families have the support they need. They can't just leave patients to fend for themselves during the process. There needs to be an ongoing system that provides consistency. Companies should be very clear with expectations, promises, and what can go wrong in an easy-to-understand format — no medical jargon.

MELISSA ADAMS VANHOUTEN
AGMD Patient Education and Advocacy Specialist; Association of Gastrointestinal Motility Disorders (AGMD)
Gastroparesis; Digestive Motility Disorders
@MelissaRVH

If asked to provide input in a clinical trial, I could provide insight as to the symptom burden, barriers to participation in my community, and the overall attitude toward pharma.

Practical factors often overlooked by sponsor companies include hardship of travel, fear of stopping current medications, and frustration at not being given results of the trial.

Technology & Patient-Focused Trials


Kevin Julian


Jim Munz


Karin Beckstrom


Dr. Bill Byrom

Technology plays a key role in helping to make clinical trials patient-centric, industry experts say. Many of the world's top biopharmaceutical companies are using new technologies to bring more of the voice of the patient into the clinical development process.

"Thanks to digitalization, it has never been easier to engage with patients and include their voices in the clinical trials process," says Kevin Julian, senior managing director, life sciences, Accenture. "We know that patient compliance and retention are critical to the success of every study, and digital solutions that improve engagement with and focus on the patient can address some of the most-reported reasons for clinical trial attrition. Is the trial site inconvenient or do patients often forget their appointments? Remote patient monitoring can reduce the number of visits and alleviate schedule conflicts, and virtual digital coordinators can handle travel logistics, for example Uber Health, and send reminders. Was the patient unclear about expectations for their role in the clinical trial, or do they feel unappreciated? Digital feedback and engagement can improve understanding and offer opportunities for encouragement and support."

Technology advances are moving rapidly, and there are some very exciting and advantageous new tools available today — and on the horizon — that sponsors can incorporate into their trials to achieve these goals, says Jim Munz, VP, eCOA product management, ERT.

"Sponsors that leverage these advances in their patient-focused study designs can simplify clinical trial participation, which improves patient engagement throughout the clinical trial," he says. "For example, by enabling patients to use messaging on their phones to communicate what they're feeling throughout the trial experience, sponsors keep patients better engaged while capturing a critical dialog to drive positive patient outcomes."

Karin Beckstrom, senior product manager, ERT, says for some patients, participating in clinical trials can seem a daunting experience. The demands of frequent investigative site visits and sometimes daily data submission may be enough to discourage them from participating, even if the trial might open doors to treatment options otherwise unavailable to them.

"But today's advanced consumer technologies are enabling sponsors to be more patient-focused in how they collect important study data," she says. "Consider, for example, how voice assistant (VA)-enabled smart speakers such as Amazons Echo can be a game-changer here. Many clinical trials require patients to complete questionnaires on either paper-and-pencil diaries, or electronically via smartphones, tablets, or desktop applications, which can be burdensome to some patients. But this burden can be overcome with voice assistant technology. Through a customized skill, the smart speaker can recite the study questions audibly and record patients' verbal responses, making it easy for them to submit this information throughout clinical trials."

Bill Byrom, Ph.D., VP, product strategy and innovation, CRF Bracket, says there is increasing interest in how trial participation can be simplified. "This includes the use of technology for informed consent to ensure study information is conveyed effectively and in an engaging manner, enabling some study visits to be conducted remotely, for example, home nurse visits or video-enabled visits, to reduce travel requirements, brokering study transportation when needed, provision of study apps and communications to help keep patients engaged and prepared during the study, and provision of lay summaries of study results and personal data to provide additional value."

> The area where patients have the most direct impact in the drug development process is helping to accelerate the clinical trial recruitment process.
>
> **FABIO GRATTON**
> CureClick

In the past, organizations developed patient-centric strategies without patient involvement, but patients are now included in defining corporate practices for enterprisewide patient-centricity. Similarly, patients are being engaged via patient surveys and interviews to understand general perceptions of clinical trials, the perceived burden of typical trial procedures, or to assess interest in providing health information for trial matching purposes.

Patients have successfully contributed to protocol development, providing input on study schedules, comparator arms vs. placebo arms, site interactions, and thoughts about the virtual-clinical trial setting.

"In some cases, patients are even serving as co-investigators to be part of the study development and delivery process every step of the way," says Marie Lux, senior director, global patient and site solutions, IQVIA. "In one recent example, a patient participated in the development of a study protocol and the assessment materials that were later used to gather patient experience feedback. Pharma companies and their partners are conducting patient focus groups and organizing advisory boards to elicit patients' perspectives on specific questions, as well as to consider long-term patient needs across programs. While insights may seem most critical prior to study start, patients can also provide valuable feedback during the conduct of a trial regarding their engagement with site staff, adherence to the treatment regimen, and experiences with specific procedures and timelines."

Patient-focused drug development de-

mands a thorough understanding of what is truly important to the patient — for example, which treatment benefits matter most or which side effects can be tolerated in trade-off for certain treatment benefits, says Bill Byrom, Ph.D., VP, product strategy and innovation, CRF Bracket.

"This not only focuses target drug profiles, but also helps to determine and prioritize the endpoints collected in clinical trials," he says. "This understanding guides the selection, adaptation, or development of patient-reported outcomes measures that should be included, in addition to other measures. For example, a factor that may be highly important to a patient suffering from COPD may be his or her ability to walk to the local shop or to escort a grandchild to school. This may lead to the inclusion of a wearable tracker into clinical protocols to enable treatment-related improvements in activity to be measured."

When patients are truly engaged and empowered in the clinical trials process, evidence shows that trial efficiency improves, Ms. Lux says.

"We know that patients today are often actively engaged in the management of their own care and study sponsors can see the value of listening to patients and learning from their experiences and expertise," she says. "By drawing from this experience sponsors can augment scientific and medical knowledge and better understand issues of prime importance to those patents."

Ms. Lux says by actively engaging patients to share their stories, perceptions, concerns, and desired outcomes, studies can be designed with the patient needs in mind. Providing this platform and two-way communication can help patients feel better connected and valued.

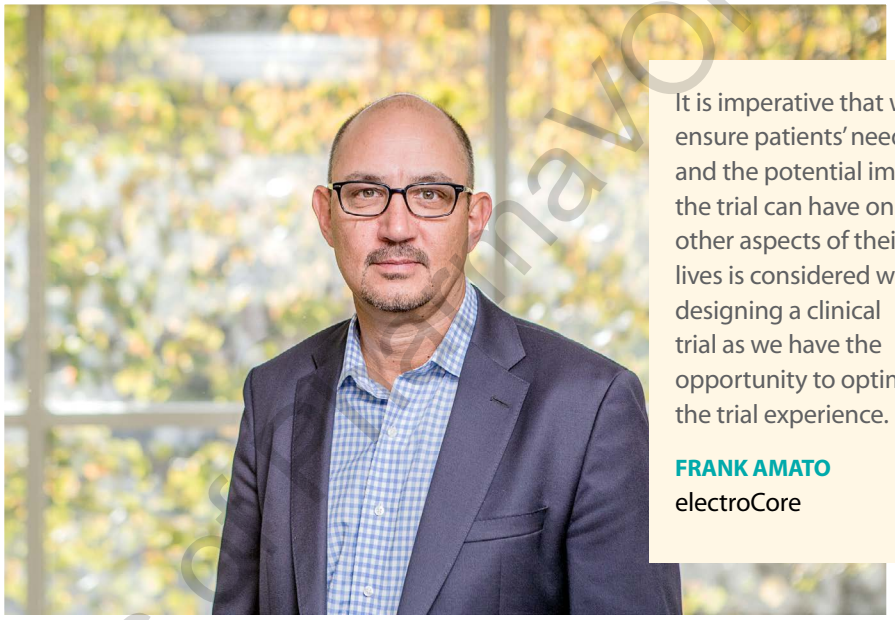
A patient-centric approach to the clinical trial process will better inform clinicians on what is important to the patients who will eventually receive the medications they are developing, says Sara Ray, senior director of research, Inspire. (Please turn to the intro for results from a recent Inspire survey.)

"In the same way healthcare providers are subject matter experts in the clinical aspects of an illness, patients are subject matter experts in the experience of their illness," she says. "They, therefore, can offer insight into daily challenges, as well as what is of value to a patient from both a trial and a new medication perspective. Patients can offer unique solutions for their challenges and needs based on their experience."

Additionally, caregiver input should be sought. Caregivers serve many roles in the clinical trial process. They can serve as the gatekeepers for information as the researchers who painstakingly collect and sift through trial information. They may take on an initial or growing role in logistics, acting as secretaries who schedule appointments or arrange transportation and accommodations. Further, they are the support system of the patient, helping to navigate side effects, fears, and are the first person the patient may turn to at times of stress. Understanding the vital role caregivers play and what would best help them fufill that role can help streamline the clinical trial process and improve the clinical trial experience.

When patients are truly engaged and empowered in the clinical trials process, evidence shows that trial efficiency improves.

MARIE LUX
IQVIA

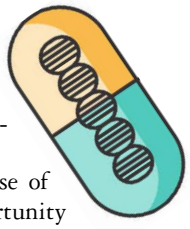


It is imperative that we ensure patients' needs and the potential impact the trial can have on other aspects of their lives is considered when designing a clinical trial as we have the opportunity to optimize the trial experience.

FRANK AMATO
electroCore

From the very beginning, patients can spot potential pitfalls in a clinical trial protocol that can harm recruitment and retention rates. "Patients can advise on which aspects of a trial may be overly burdensome and might impact retention," Ms. Ray says. "They can also inform which aspects of the trial are motivating and would increase likelihood of recruitment and retention."

In addition, patients can help clinicians understand how to better communicate their protocols to potential participants. Using the patient lexicon and providing information that is most valued in an accessible way can make a huge difference to patients and caregivers who are often overwhelmed with their diagnosis, bombarded with information, and facing extremely important and time sensitive decisions.



Some experts say, with the use of patient input comes the opportunity to revolutionize therapeutic development, particularly within rare diseases.

"With patients contributing their experiences and perspectives through patient experience data (PED), patient perspective information (PPI), and other real-world evidence (RWE), clinical trials and the ensuing therapy are substantially more patient-centric," says Paul Melmeyer, director of federal policy, NORD. "This means the therapy treats the specific symptoms the patient populations desire to be treated, the side effects are tolerable, and the benefits clearly outweigh the risks. This also means clinical trials are patient-focused: endpoints are meaningful to patients and their everyday experience, trial designs are accessible and not overly burdensome and accommodations are made to allow for patients and their families to comfortably participate. This is all possible due to the advent

of patient-focused drug development and the myriad data that is now being collected from patients and their loved ones."

Mr. Keens says anecdotal evidence supporting the positive benefit to trial recruitment/enrollment derived from patient feedback and a patient-centric approach continues to accumulate. "With increasing frequency, sponsors are expanding opportunities to involve patients upfront in their protocol creation, and discussions within the drug industry of decentralized or virtual clinical trials are much more prevalent at conferences and industry publications than even one year ago," he says.

In an informal survey conducted by Firma Clinical Research, when clinical trial patients were asked if the "option of home health visits directly influenced (their) decision to participate in the clinical trial," more than 90% of patients answered "yes."

Patient Input Can Help Clinical Trial Designs

Bioharma and medical device companies, and even the Food and Drug Administration are including more patients and advocacy

Pharma Company Patient-Focused Efforts

PharmaVOICE tapped a number of pharmaceutical company executives to learn about their approach to patient-centric drug development.

KAROLY NIKOLICH
CEO, Alkahest

Alkahest is a clinical stage biopharmaceutical company dedicated to treating neurodegenerative and age-related diseases with therapies targeting the aging plasma proteome.

People living with certain medical conditions are uniquely positioned to inform the understanding of the therapeutic context for drug development. At Alkahest, we have followed this model and only focus on the most critical age-related diseases such as Alzheimer's disease, Parkinson's disease, and age-related macular degeneration. We believe it is important to take every aspect and stage of the disease into consideration when developing the trial design. We hope that involving patients, caregivers, and advocates from the start allows us to work to develop other primary endpoints or trial goals that will lead to a positive impact on patients' quality of life.

Alkahest includes patients in team meetings or company events so that staff members have a chance to understand, connect, and learn from them. They can highlight which factors they take into account when making decisions about a course of treatment and their experience with current treatments, which is extremely valuable information when designing a clinical trial.

PUSHKAL GARG, M.D.
Chief Medical Officer, Alnylam

Alnylam is leading the translation of RNA interference (RNAi) into a new class of innovative medicines with the potential to transform the lives of patients who have limited or inadequate treatment options.

We have been participating in the FDA Patient Focused Drug Development initiative using the information coming out of these patient voiced meetings as part of the drug development for hereditary ATTR (hATTR) amyloidosis and for porphyria. Our first product, Onpattro, has been approved for hATTR amyloidosis, rare disease that is progressive and frequently fatal.

Our pipeline includes givosiran for acute hepatic porphyria. The endpoints for our recent trial were selected based on data from patient-voiced meetings and patient interviews. We thought patients were most concerned about acute attacks, but one of the big revelations was that between attacks, they have disabling chronic symptoms that limit their ability to work or go to school and it has an impact on their social lives. That was something we built into our Phase III trials.

NASSIM USMAN, PH.D.
CEO, Catalyst Biosciences

Catalyst is a clinical-stage biopharmaceutical company developing novel medicines to address hematology indications. The company's lead product, which is in Phase II/III trials, is a subcutaneous prophylactic Factor VIIa (FVIIa) variant marzeptacog alfa (activated) (MarzAA) currently being developed for the treatment of hemophilia A or B with inhibitor.

We believe it's critical to be patient-focused in rare disease because there are so few patients. We work with the Hemophilia Society and with patients to understand what their needs are.

We want to understand the real-world use of drugs. We speak with patients. We speak extensively with the key opinion leaders or the physicians who are the leading researchers in the field in terms of clinical medicine. It's very important for us to talk to both patients and physicians because they're the ones who deal with their disease on a daily basis and we want to make sure that we are tailoring our drugs or our clinical trials to meet their needs.

ALEX OVADIA
CEO, Check-Cap

Check-Cap is a clinical-stage medical diagnostics company advancing the development of C-Scan, the first and only preparation-free ingestible scanning capsule-based system for the prevention of colorectal cancer through the detection of precancerous polyps. The company recently received approval to initiate a U.S. pilot study of the C-Scan system at the New York University School of Medicine to initiate a U.S. pilot study of the C-Scan system.

We are very sensitive to patient-oriented requirements. We identified an unmet situation and initiated a comprehensive program to resolve it. The main target was to provide a solution around the patient while thoroughly considering the barriers, which make patients unwilling to go through routine procedures.

FRANK AMATO
CEO, electroCore

electroCore is a commercial-stage bioelectronic medicine company dedicated to improving patient outcomes through its platform's non-invasive vagus nerve stimulation therapy. The company's gammaCore (nVNS) is a hand-held medical therapy FDA-cleared as an adjunctive therapy for the preventive treat- ▶

groups in discussions regarding clinical trial design and primary study endpoints.

Chris Trizna, president, CSSi, believes not enough time and research are put into understanding the world of the patient. "We develop clinical trials with study visits, procedures, and other requirements based on endpoints and clinical data," he says. "But without understanding the patient world, study visits and procedures make it difficult for a patient to participate in a study. As an industry, we need to listen to the patient and understand their world, but also include the caregiver, medical professionals working with the patient, and listen to advocacy groups more."

CSSi has developed a platform that includes the voice of all people associated with specific conditions.

"We are able to survey patients on everything from their personal challenges to their thoughts on study visits and procedures; we involve sites and other medical professionals to get their opinion, and evaluate de-identified EMR data on patients and their views of the protocol; and through the advocacy groups we are able to better understand the challenges and needs of the patient," Mr. Trizna says.

Pharma Company Patient-Focused Efforts

▶ ment of cluster headache and as an acute treatment for pain associated with episodic cluster headache and migraine headache in adult patients.

As a company developing alternative therapies for these patients, it is essential that we have a clear understanding of why current treatment options do not meet their needs. In this case, our patient-focused development process has allowed us to learn that these individuals need safer, more efficacious therapies with fewer side effects.

LEWIS BENDER
Founder and CEO, Intensity Therapeutics

Intensity Therapeutics is a clinical-stage biotechnology company pioneering a new immune-based drug approach to treat solid tumor cancers. Its lead product, INT230-6, is currently in human clinical testing to treat refractory solid tumor cancers.

Everything that drug companies do should have a patient-centric direction and every decision should consider whether the resulting action will benefit patients and how. This is the premise on which I started the company. And this is how we make development decisions.

HAROUT SEMERJIAN
Executive VP, Chief Commercial Officer, Ipsen

Ipsen is a global biopharmaceutical group dedicated to improving lives through innovative medicines in oncology, neuroscience, and rare diseases.

We're using a combination of patient-centric initiatives, such as advisory boards, value delivery models and patient/physician apps, to understand how we can best support patient needs as these needs sometimes change over time. This has become a normal part of our business and represents an important cultural shift, whereby every new project starts with patients in mind, and success is measured from that perspective.

Patient advisory boards, in particular, play a big role in Ipsen's efforts. We recently organized advisory boards to hear directly from acromegaly patients, who represent a very niche population. Based on the insights gained from the boards, we interviewed more than 200 patients and nurses, we found that patients were facing challenges with the syringe design of our product. For example, acromegaly patients, who typically have bigger hands, found the small size of the syringe difficult to use and requested we find ways to make it more ergonomic. With that knowledge, we designed a new syringe, approved and manufactured for all markets, which, among other patient-inspired features, is much bigger and more robust.

MICHAEL DUNNE, M.D.
Chief Scientific Officer, Iterum Therapeutics

Iterum Therapeutics is a clinical-stage pharmaceutical company developing anti-infectives against multi-drug resistant pathogens. The company's lead compound, sulopenem, is a novel penem anti-infective compound in Phase III clinical development with oral and IV formulations.

Iterum is doing more than just asking patients about symptoms in its development programs, but also how those symptoms actually impact patients' daily lives — are they bothersome, debilitating, limiting activities of daily living, and so on. These types of questions aren't usually seen in development programs. Normally, patients are asked to rank their symptoms on a scale of 1 to 5. We are exploring how to make this information on patient impact available to regulatory reviewers and to the physicians who make decisions about antibiotics use. We are also considering packaging the data in a way that is interesting and relevant to patients, who ultimately are the reason we do what we do.

The company's focus groups with patients also address their experiences with physicians. Some patients who have recurrent but otherwise uncomplicated infections don't always feel that they get the attention their infection deserves because doctors are busy and may be dealing with life-threatening conditions. But patients who have recurrent episodes of infection may need more support than they're getting. When our teams are in the field we will try to help remind physicians of the challenges that women with UTIs endure as they go about their lives.

ELAD KEDAR
CEO, Orasis Pharmaceuticals

Orasis Pharmaceuticals is a clinical-stage pharmaceutical company developing a corrective eye drop for the treatment of presbyopia as an alternative to reading glasses.

Patients' input was used to help the company design of some of the clinical trial protocols for its lead compound. It is essential that study protocols be designed using patient input as it ensures that the drug candidate is being evaluated in realistic circumstances and as it would be used by the patients if it were to be approved. This will ensure that real-world outcomes more ▶

"Patient input is crucial to both the drug development process and clinical trial protocols," says Christian Homsy, CEO of Celyad, a clinical-stage biopharma company focused on developing CAR-T cell-based therapies. "It helps industry understand the real-world implications of certain treatments and allows us to develop protocols and clinical trial endpoints that truly benefit these populations while also working with regulatory agencies to ensure that the protocols and endpoints can be used for ultimate drug approval. We are in a day and age where patients are more invested and educated about clinical trials than ever before and their feedback is crucial to truly understanding the lifestyle of a population in order to develop a cost-effective, convenient, and effective clinical trial. The voice of the patient is also important in promoting open communication between industry, doctors, and principal investigators and lets patients voice what truly matters to them."

Incorporating the patient voice into drug development allows the industry to design better clinical protocols, which in turn can lead to better recruitment and enrollment, and inform FDA's regulatory decisions on new therapies, says Clareece West, VP/general manager, Cardinal Health Regulatory Sciences. "From gathering new perspectives in FDA-initiated patient meetings to crowd-sourcing patient experiences for greater insights, science and patient data are becoming virtually inseparable in today's fast-paced global development environment," she says. "In my 30-year-plus career, patient engagement has never been

Pharma Company Patient-Focused Efforts

▶ closely reflect what is demonstrated through clinical trials outcomes.

In working to develop a therapy that aims to alleviate the burden of current treatment options, our work must be deeply rooted in enhancing our understanding of the impact those treatment options can have on patients' lives and how and why current treatment options are not adequately meeting those needs.

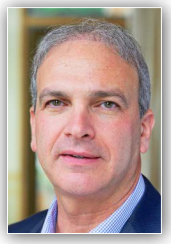
PATRIK DE HAES, M.D.
CEO, Oxurion

Oxurion is a biopharmaceutical company developing innovative treatments to preserve vision in patients with diabetic eye disease.

The company continuously engages with patients through partnerships with patient advocacy groups, such as Prevent Blindness and Retina Global. In doing so, we are transforming the idea of patient-focused drug development from an aspiration to an ongoing company activity, which leads to the patient becoming more naturally integrated into our activities and development processes.

Therapies that require a frequency of treatment that can interfere with other aspects of a patient's life are often underutilized, which is why patient input must be considered as a part of the development process.

Clinical trial design should take into account the burden placed on the patient during the clinical trial process and aim to create an engaging experience for the patients who are committing their time and energy to the process.



RAMI LEVIN
President, North America, Sobi North America

Sobi is an international biopharmaceutical company dedicated to rare diseases.

In rare diseases, it's important not just to bring medicines to patients but also to help meet the needs of patients beyond just medicine. We have created and developed a patient-support program that is tailored to patients' needs.

For example, for Orfadin, the company recognized the need to provide either guidance or dietary support as part of the services it offers to HT-1 patients.

The company is now launching Gamifant (emapalumab-lzsg), an interferon gamma blocking antibody for the treatment of pediatric (newborn and older) and adult patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance to conventional HLH therapy.

We are now assessing what patients' needs are so we can build and develop a patient-support program to try to address them.

To be truly focused on patient needs, companies have to create a patient-centric culture. This reminds everyone why we got into the pharma industry to begin with, and why we are in rare diseases specifically. Also, it is critical to interact with patient organizations to understand patient needs as we develop programs and services. As part of our culture, we make sure we make decisions always with the patient in mind.

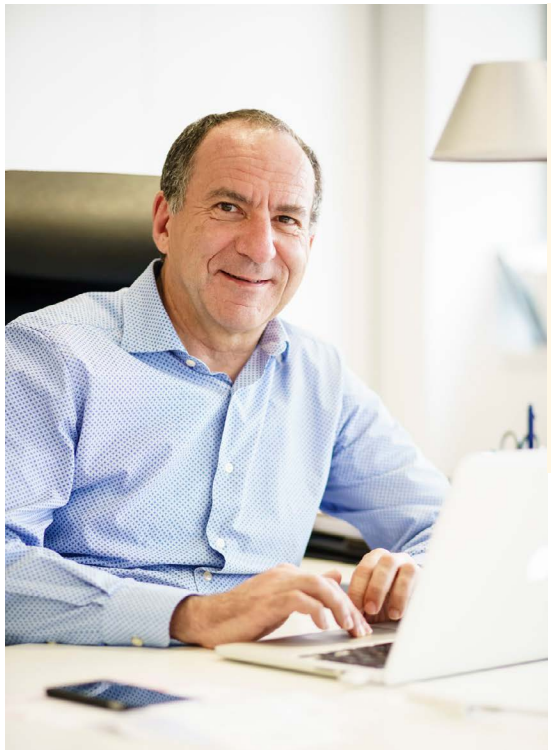
Sobi also created a patient advocacy function to reach out to all the different advocates in specific disease areas. We make it a point to meet regularly with these groups to understand their needs, to see how we can collaborate, and to see how we can help and support them. For Gamifant, we organized a patient summit and brought all of the different patient organizations that touched these primary HLH patients together for a day and a half workshop to truly understand what the patient journey looks like, what their needs are at every stage, and make sure that moving forward we can collaborate and work with them as we built our programs to address those needs. In the rare disease space, the patient voice has grown in importance over the years helping to us to focus on what we do.

ROBERT DERHAM
VP, Orphan Products Q BioMed

Q BioMed has assets in oncology, vascular disease, and rare orphan diseases that address unmet medical needs and large markets.

One product in the company's pipeline is QBM-001, which is being developed to help treat the rare subset pediatric non-verbal autism. Q BioMed has been working with Autism Speaks, which organizes town meetings with both parents and different types of caregivers, as well as psychologists and educational specialists.

This is key, especially when working with children who are nonverbal or minimally verbal. This has led us to adapt how the product will be administered to provide parents and caregivers the flexibility they need. It has also led us to taking extra time to formulate the products and also to identify biomarkers that could eventually lead to a companion diagnostic to further ensure the best outcome for the children.



> We are in a day and age where patients are more invested in and educated about clinical trials than ever before and their feedback is crucial to truly understanding the lifestyle of a population in order to develop a cost-effective, convenient, and effective clinical trial.
>
> **CHRISTIAN HOMSY**
> Celyad

higher, and we have yet to maximize its fullest potential."

Patient-focused drug and medical device development is an integral part of the clinical development process as it provides companies with a better understanding of a patient's needs and how a disorder or condition impacts his or her everyday life.

"This is a particularly important aspect of the development process for medical device companies; it allows for a deeper understanding of how patients will consider both the benefit and burden when choosing whether to integrate a therapeutic device into their treatment routine," says Frank Amato, CEO of electroCore.

Patient engagement also assists in the identification of benefit-risk outcomes. "This can be pivotal in developing clinical outcome assessment tools or patient-reported outcome measures for clinical trials that more accurately capture the patient's perspective," he says.

Ms. DeCotiis says companies are implementing detailed, patient-focused protocols so that patient engagement is viewed as a long-term investment with sufficient and sustained resources to reproduce outcomes.

"This way companies can identify patient-centric endpoints and patient-relevant outcomes for clinical trials that, in turn, lead to more relevant therapies," she says. "Patients can also become partners in seeking regulatory support, collaborate for increased awareness, and review lay publications, patient materials, and communications. By valuing patients' insight and input we can build a relevant and meaningful patient-centric process that meets the needs of regulators."

Patient input is increasingly being taken into consideration in the development of clinical trial protocols, but there is much more that can be done to make such input systemic and scalable, says Kevin Julian, senior managing director, life sciences, Accenture.

"For the most part, clinical trials are oriented around treatment in the context of the research facility, not around the patient," he says. "Redesigning the entire process around the patient experience, from intake to last treatment, and moving from paper-based reporting to more user-friendly mobile and digital reporting, will have a real impact on patient satisfaction and retention. Even before the clinical trial, there are opportunities to bring the patient voice earlier into the development process to help identify barriers to adherence, including challenges that patients face during treatment."

Mr. Julian says Accenture is working with its biopharmaceutical clients to proactively bring the voice of the patient — data about and stories from patients living with a given condition — into co-creation/ideation sessions with representatives from across the pharmaceutical value chain, to help in the development of clinical trial protocols and in the design of digital therapeutic solutions.

"These sessions are eye-openers to sponsors that aren't always aware of the realities that patients face and how that might impact the success of their treatment," he says.

Integrating patients' input can improve the clinical trial process and help to design trials that will demonstrate real-world outcomes.

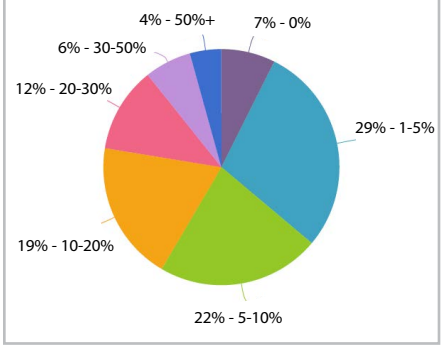
"Using those inputs, protocols can include measures that reflect what aspects of the drug are important to the patient and imitate the way in which the patient would use the drug in the real world," says Elad Kedar, CEO of Orasis Pharmaceuticals. "Developing a deep understanding of how a drug candidate has the potential to impact patients' lives is essential in defining trial endpoints that accurately capture the outcome that is experienced by the patient. For example, in developing a corrective

Clinical Trial Adherence

AiCure, an AI and advanced data analytics company targeting the healthcare industry, uses proprietary intelligent software to capture and understand video, audio, and behavioral data to establish the link between patients, disease, and treatment. The company recently fielded a survey to understand patient adherence during clinical trials. Among the more than the 105 surveyed as part of this special report, more than 80% are involved in at least one clinical trial and of this subgroup 21% are involved in five to more than 20 clinical trials. The majority of these trials are in the oncology, CNS, respiratory, cardiovascular, and gastrointestinal therapeutic areas.

Through its internal research, AiCure has found that some patients who enroll in clinical trials have no intention of taking the drug being tested. When asked if respondents have patients intentionally not taking their medications in their clinical trials, the results were surprising: **more than half — 55.1% — said yes or they didn't know. More than 75%** of respondents also estimate that between 1% and 30% of patients in clinical trials intentionally do not take their medication. The good news is that **86% said that intentional nonadherence is crticial to the success of their clinical trials,** which means nonadherence is on their radar.

What percentage of clinical trials do you think fail due to patients intentionally not taking their mediciation.



eye drop as an alternative to reading glasses for individuals with presbyopia, we have defined trial endpoints that not only measure the degree to which near vision was improved but also a set of comprehensive measures that capture the whole patient experience including factors such as onset and duration of effect."

Industry leaders say patient input should be sought before study protocol development to ensure researchers fully understand the impact of the disease and its treatment in the view of the patient, and the patient perspective on aspects of treatment such as their minimum threshold expectation of treatment benefits, their level of tolerance toward side effects and acceptable trade-offs between risk and benefit associated with treatment.

"This will guide the measurements and endpoints included in the study protocol, including the selection, adaptation and/or development of patient-reported outcomes measures," Mr. Byrom says. "In addition, a good practice would be to assess the feasibility of the study protocol in the view of the patient. This may be informative in terms of understanding the burden of study procedures or study logistics on the patient, and enabling the tailoring of these to lower barriers to participation and study completion."

Ms. Josey of VMS BioMarketing says involving patients early in drug development to assess their perception and commitment to being in a trial and taking the drug being developed is the key to compliance with the drug in the future. Even the simple action of interviewing patients in person versus sending a survey or email would be a tremendous enhancement. "Employing trained medical personnel such as nurse educators would help pharmaceutical manufacturers learn about what dosage modalities and timing would help a patient be most compliant," she says. "Talking to patients in advance about possible side effects of the drug being studied would help manufacturers understand patients' level of tolerance and help them learn what education is needed in order for the patient to enroll and stay in the trial. By discussing potential risks associated with the drug or study would help manufacturers understand patients' ability to assess risks and what trade-offs they are willing to make in their lifestyle to participate in the trial and continue to use the drug after it is approved."

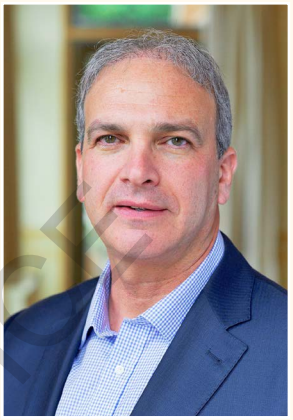
"Manufacturers and CROs must not overlook or downplay the emotional needs of patients," Ms. Josey warns. "In a recent study that analyzed 500,000 de-identified and anonymous public comments that occurred in public online forums for patients living with chronic diseases, researchers found that six of the top eight unmet needs are emotional concerns rather than medical concerns."

From the very beginning, patients can spot potential pitfalls in a clinical trial protocol that can harm recruitment and retention rates.

SARA RAY
Inspire

With the right approach, data gathering can paint a much broader picture of the patient's overall treatment experience.

PATTY ZIPFEL
MicroMass Communications



It's impossible to be in rare diseases and not be patient-centric considering the small patient populations who we treat.

RAMI LEVIN
Sobi North America

Fabio Gratton, co-founder and CEO, CureClick, says the area in which patients have the most direct impact in the drug development process is in helping to accelerate the clinical trial recruitment process.

"One of the biggest challenges organizations face when it comes to advancing medical research is completing their trial enrollment," he says. "If a company can't recruit the right number of patients, the study cannot proceed. Unfortunately, there is still a big disconnect between how companies recruit and how patients get their information. Patients with chronic conditions or rare diseases tend to get a majority of their news from other patients, and these exchanges are taking place in private forums, message boards, Facebook groups, etc. They trust what other patients say more than anyone else, except maybe their doctor. So if companies really want to find patients for their trials, they need to develop strategies that engage patients where they live."

Ms. Josey says when patient-focused drug development is being used in clinical trials, the impact is very positive in terms of enrollment and recruitment.

"Considering 48% of sites miss their enrollment targets, and 80% of trials are delayed due to recruitment, the impact manufacturers and trial sites can make in supporting the patient from informed consent to the conclusion of the trial can only be a win-win for everyone," she says. "For example, engaging a nurse educator in a patient-focused clinical trial will help find the right patients, inform the patients/caregivers more effectively, screen patients more effectively, get stronger buy-in from the patient/caregivers, help avoid delays and keep the patients in the trial until the end."

Ms. Ray agrees that involving patient expertise and experience can help pharmaceutical companies mitigate patient challenges that impact recruitment and retention.

"Efforts range from creating resources to help patients better understand the trial to helping patients navigate logistical challenges and removing aspects of the protocol that may have been nice to have, but prove to be unnecessary barriers," she says. "Patient-focused drug development can solve for these issues early on, improving the efficiency and experience of a clinical trial, which will impact recruitment and enrollment."

Most importantly, a patient-focused approach will make patients and their families feel as if they are part of the research process instead of simply subjects of it.

"When patients feel as if they are partners in something bigger, this will not only improve recruitment and retention rates, but also patients' overall experience and understanding of clinical trials," Ms. Ray says. "This positive experience will foster better relationships between pharma companies and patients, build brands, and increase engagement down the road." PV

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