

# Moving Toward a Patient-Centered Clinical Trial Model

- Clinical research is shifting toward greater patient engagement as the biopharmaceutical industry explores new ways to integrate various healthcare trends and technologies that could allow patients to become more actively involved in clinical trials. These trends have the potential to bring about a shift from the industry's current site-centric model to a more patient-centered model.
- Pfizer, for example, is re-examining not only how the company engages patients in its clinical trials and how that process can be improved, but also how patients have become more active in their healthcare decisions and what this trend's implications are for clinical research.

**A**s patients—empowered by information and technology—have become increasingly involved in their own healthcare decisions, the pharmaceutical industry has begun to look at the opportunities this trend brings for improving the productivity of its clinical development process.

The industry has already seen clinical research shift toward greater patient engagement as the widespread use of electronic patient reported outcome (ePRO) tools allow patients to record clinical data. But, today, leaders in the biopharmaceutical industry are exploring new ways to integrate various

healthcare trends and technologies that could bring about a shift from the industry's current site-centric model to a patient-centered model that could more actively engage patients in clinical research.

Pfizer has begun to re-examine not only how the company engages patients in clinical trials and how that process could be improved, but also how patients have become more active in their healthcare choices and this trend's implications for clinical research.

“An engaged patient that is well-informed creates opportunities for us to rethink how we are approaching and recruiting those patients, how we are informing and consenting patients, how we are collecting and sharing data and information,” said Craig Lipset, director of Clinical Research at Pfizer. “Overall, I view this as an opportunity for our industry to evolve from enrolling clinical trial subjects to true clinical trial participants.”

Once all safety and regulatory concerns are addressed, a patient-centered model—which integrates mobile and Internet-based technologies, along with the principles of telemedicine and the tools of health information technology—could potentially allow patients to participate in a clinical trial entirely from their homes.

“As long as we are able to demonstrate, first and foremost, that patients are being protected, that their safety is

being rigorously monitored and that they are protected from an ethical standpoint, then I believe that the tools exist in healthcare to demonstrate that we can monitor patients remotely today. This is being demonstrated in healthcare with telemedicine. As the population continues to age, it is increasingly important for the future of healthcare to be able to monitor patients continuously in an ambulatory or home setting. As long as the patients' welfare is being protected and you can ensure compliance with appropriate federal and state regulations, then there is the potential to have patients participate in clinical trials without a physical site," Lipset said. "This is something that we can aspire to and make happen, and not over a very long-term horizon."

## Patient-Centered Trials

The idea of patient engagement in clinical trials mirrors trends that have emerged in healthcare. In particular, patients today are not only more informed, but they have become more active in their healthcare decisions, mainly by participating actively in dialogue with their physicians about their health. In addition, there is increasing adoption of electronic health records (EHR), making it possible for patients to access their own health information online.

"Overall, we are seeing a shift within biopharma in thinking that the patient's perspective is as important as the physician's perspective. Fifteen years ago, it was all about the physician. Now there is a trend where there is a partnership between the patient and the physician in determining if a therapy is really helpful," said Philip Lee, president and CEO of PHT, a company that provides ePRO solutions. "There is a huge trend toward more patient-centric medicine. That is what this is all about."

Recent studies show a rise in patients tracking and monitoring their own

health information and sharing that data online using social media and Web 2.0, including user-generated content, blogs and podcasts. "When patients are able to quantify their health and share that with others online, it enables a paradigm that we see at sites such as PatientsLikeMe.com and CureTogether.com where patients are able to conduct their own research. Once patients are quantifying information about themselves and sharing it in a common database with one another, you have this phenomena of open source research or patient-generated research, where patients themselves are self-organizing and answering research questions by building their own structured quantitative data sets," Lipset said. "There are exciting and interesting things going on in healthcare, which raises the question: 'What are the implications, the opportunities, and the risks in terms of how we are conducting regulated clinical trials today?'"

## Tools for Patient-Centered Trials

Clinical research has begun to shift toward greater patient engagement in recent years as the availability of ePRO and other technologies has made it easier to involve patients directly in clinical research.

Pfizer, for example, recently entered into a partnership with Private Access, a company that provides technology that makes it safe for medical records and other personal information to be accessible over the Internet, to create a new online community aimed at increasing clinical trial awareness and participation, along with making sure patients feel comfortable and secure about sharing health information with researchers.

In another example, Quintiles developed a virtual clinical research community of more than 2 million patients, who have agreed to

volunteer or provide insights and guidance to advance clinical research, through a proprietary web site called iGuard.org. Quintiles launched iGuard about two years ago as a medication monitoring service designed to help patients get personalized safety alerts for their medicines. In return for a free medication monitoring service, members provide data to Quintiles that can be used to inform decisions about participating in clinical research.

"As part of the changing landscape in the biopharmaceutical industry, patients are taking control over decision-making about their treatments, including whether to participate in clinical trials, as they access a wealth of information on the web," said John Ratliff, chief operating officer at Quintiles. "With more than 2 million participants, iGuard gives Quintiles unique access to data that can really inform the way we conduct clinical research. We can help our customers identify potential risks before their studies begin, driving productivity and accelerating outcomes. We can rapidly reach out, directly, to patients before deploying a protocol and ask them if they'd like to volunteer to answer a number of questions upfront."

In addition, there are established ePRO tools that patients already use to capture data in a clinical trial. Patients can use the Internet, telephone-based interactive voice response systems, handheld PDAs and mobile phones to record data that can be electronically transmitted to study sponsors. "From the technology standpoint, ePRO enables a view of the patients between visits, which, prior to having electronic data capture for patients at home, really wasn't possible. ePRO enabled a lot of possibilities for patients to have a more active role potentially in their outcomes as well as in the trial," said Sheila Rocchio, vice president of marketing for PHT.

Many ePRO companies were founded, in fact, with the idea of allowing patients to participate more directly in clinical trials. "Our mission as a

company from the start has been to really restore the place of the patient in clinical research and give the patient a voice by applying these methods we bring to the patient-reported outcomes piece of clinical research,” said Doug Engfer, founder, president and CEO of invivodata. “The work that we have done as a company certainly reinforces that, yes, you can engage patients in research, you can get them to do what you need them to do, you can get good data from patients and they will engage and participate in a meaningful way. And you can get data out of that to help get your drugs approved.”

The importance of a patient’s point-of-view in a clinical trial was reinforced by a U.S. Food and Drug Administration (FDA) guidance issued in December, which finalized a draft guidance published three years ago, that defined patient-reported outcomes (PROs) and gave recommendations on how sponsors can use study results

measured by PROs to support claims in medical product labeling. “When PHT was founded in 1994, our founder was really interested in this idea of giving patients a way to self-report data more accurately and giving researchers a stream of data that was more reliable and could be a more longitudinal look at [how] patients were doing over time given different therapies. We’ve been a part of that for a long time, and the draft guidance gave more credence from a regulatory standpoint on the importance of patient data, and then the final guidance gives sponsors a more formal framework for how the agencies are interested in analyzing that data for approval,” said PHT’s Rocchio.

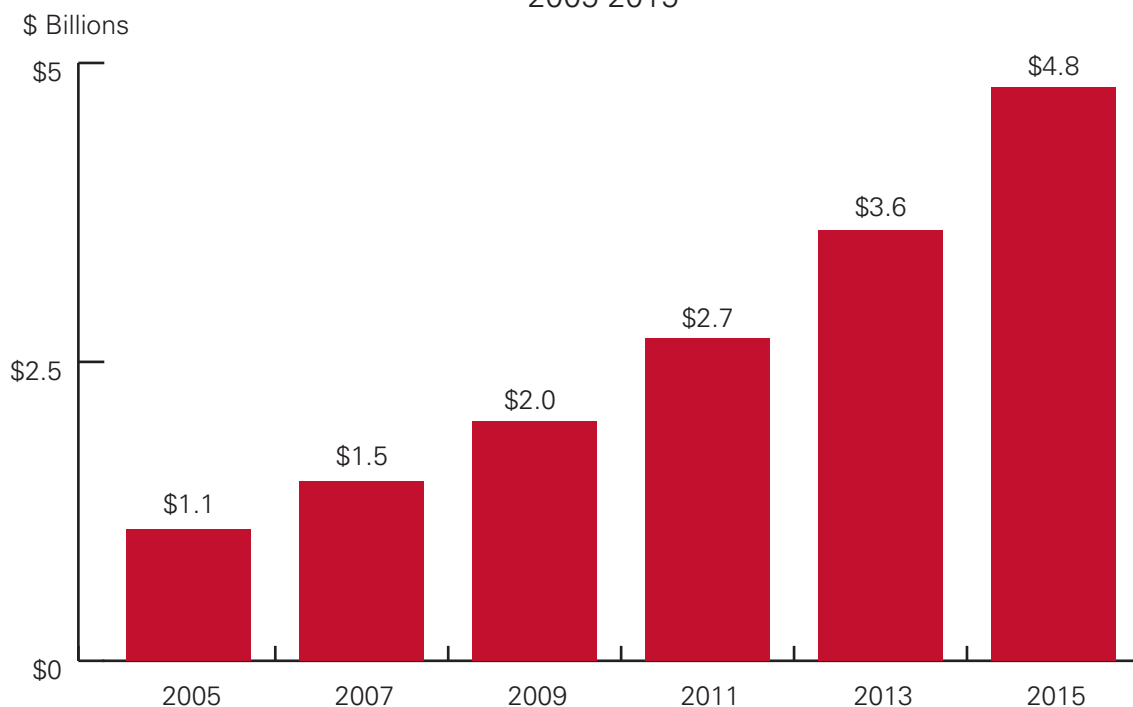
Other tools used in the healthcare space, such as physiological monitors that can capture data directly from patient activity (e.g., quality of sleep) are increasingly being used in the clinical research space. In addition,

commercial products, such as the Fitbit, which allows consumers to track fitness and health data, also have become popular tools. Pfizer and other drug sponsors are using these types of sensors in their clinical trials and are developing novel algorithms to be able to answer important questions about efficacy and safety in their medicines.

“When we start to look at trends today in health and wellness where individuals are self-tracking and using tools such as iPhone applications to track their nutrition, fitness and health information, we start to see similarities to ePRO and can explore how these two worlds can start to converge. We are seeing the same type of patient reporting going on in both parallel worlds,” Lipset said.

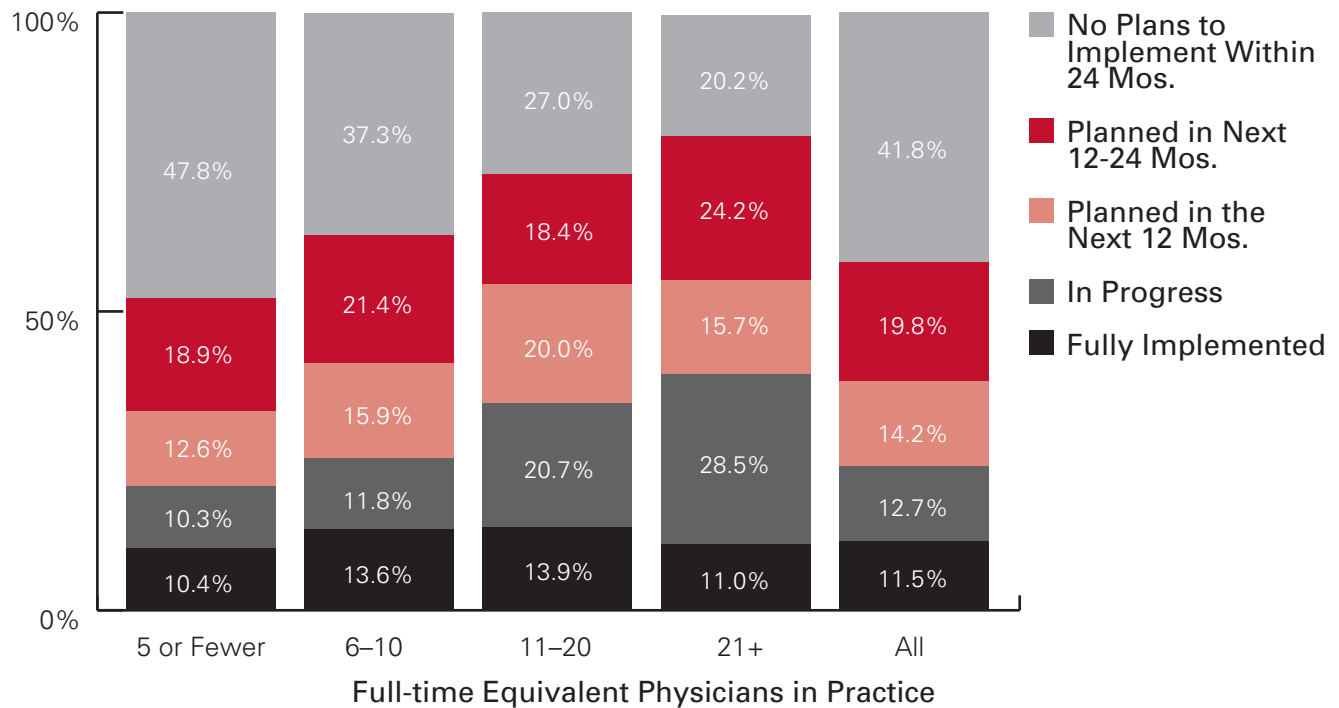
Many ePRO systems already can connect to different sensors or devices that a clinical trial participant uses at

### Estimated Electronic Health Record Market Growth 2005-2015



Source: Health Industry Insights, 2006

## Electronic Health Record Uptake By Practice Size



Source: Assessing Adoption of Healthcare Information Technology, 2005, MGMA

home, such as blood pressure monitors or glucose meters. “We are seeing more of that type of capability to connect different devices that a patient might be using,” said PHT’s Lee. “We’ve designed a communications backbone that uses Bluetooth and other things. If there is a new type of measuring device you want us to integrate, then we just have to evaluate that and get it done. It’s a pretty open system.”

Additional technologies that can help facilitate direct patient involvement in clinical trials are expected to emerge in the future. As Lipset has begun to talk at conferences and other public forums about the trends that make a patient-centered clinical trial possible, companies that offer innovative technologies for the telemedicine space and other aspects of healthcare are starting to see opportunities to repurpose their technologies for use in a patient-centered model for clinical research.

“The world of telemedicine already includes technologies to meet many patient monitoring needs. If we can create an ecosystem like an apps store [using the concept of iPhone applications] where people can come in with those technologies to fill our clinical trial needs in a compliant manner, we will be able to further extend our engagement with patients in creative ways,” Lipset said.

While a patient-centered clinical trial model could help a drug sponsor save time and money, the financial implications remain unknown, as many of the potential benefits from this model are hard to quantify. For example, if a drug sponsor could improve study design by using patient information for hypothesis generation or if patient groups were involved in testing ePRO instruments used to collect data for a trial, the result could be better trial execution, improved recruitment, improved

retention, improved compliance and, in the end, improved data quality.

“A better engaged patient should be easier to recruit, easier to get quality data from, and more likely for the patient to persist in the trial over time. If we have a patient that feels engaged as a partner in the clinical trial, these soft endpoints, which do have real cost implications, can be very important,” Lipset said.

### Implications of Patient-Centered Trials

As mobile and Internet technologies improve, the once far-out idea of at-home clinical trials becomes more of a reality. “That is possible, and I think that we are seeing a shift toward that.

You always want a physician monitoring the patient. If they are taking a drug, you do want some oversight, but I don't think you need the overhead of having a physical site where people go every week and meet with the doctor. That is not as necessary. With the advent of technology, it shows that you can get a continuous stream of how the particular medication is affecting the subject on a daily basis and then only reach out to the patients where you think it necessary. It doesn't become a routine thing. I think it is more cost effective," said PHT's Lee. "With the electronic devices we use, the data is always up-to-date. It really enables this mode of clinical trial much more strongly. If they were collecting data on paper, this would not be possible."

While regulatory hurdles must be cleared before a drug sponsor would be able to conduct a randomized clinical trial that allows patients to participate entirely from home, Phase Forward already has been involved

with post-marketing and observational-type programs that are purely web-based, where a physical investigative site is not involved.

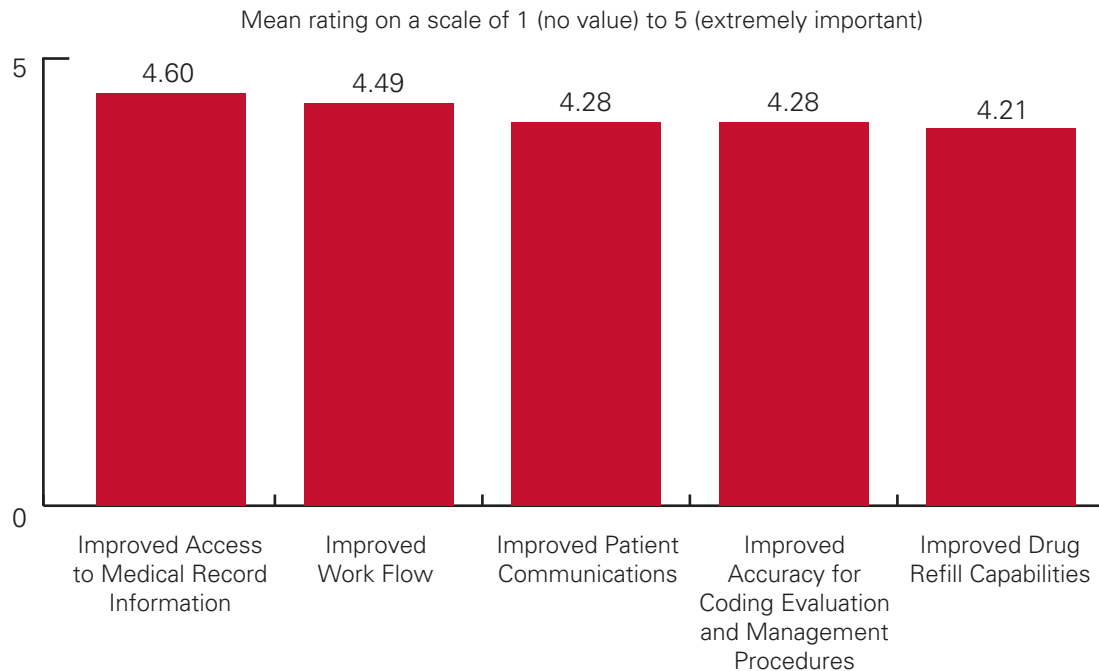
"These studies are looking at proof-of-concept to say, 'What does the overall disease state look like?' or 'What is the patient population feeling or experiencing?' They could be on any therapy or multiple therapies. We've already done some of that via the web with our technology," said Scott Dixon, vice president, Global CRO Partnerships, Phase Forward.

The trend toward greater patient involvement in clinical trials also can result in the need for fewer patient visits. "We at Phase Forward are not advocating taking an investigator completely out of the loop. You need oversight. But you don't have to have the patient in as routinely because, at some of those visits, they are just checking drug supply and asking how the patient feels, which

you can check remotely now. You can reduce the amount of patient burden without adversely affecting the patient's safety or completely removing the doctor," Dixon said. "I think you will start seeing some shifts from where, instead of having 12 visits, you only need four or five patient visits."

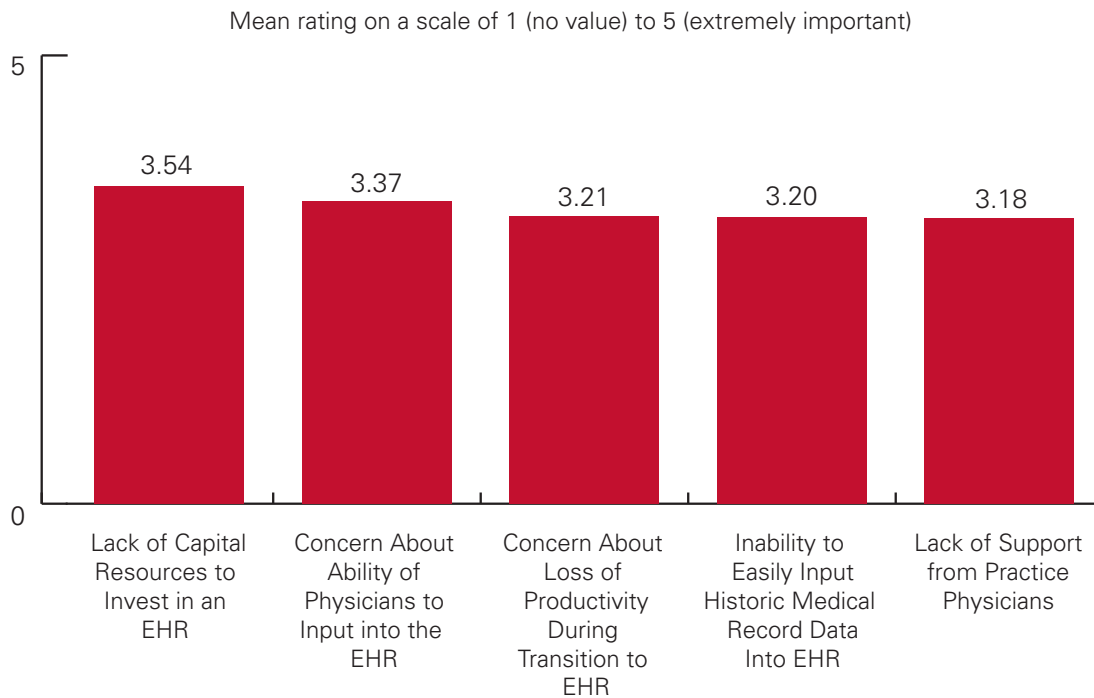
PHT is working on an observational trial in Europe that includes an investigative site, but the required patient visits to the site are infrequent. "I don't think you need to do away with the visits completely, but if you did it once every six months instead of once every two weeks, that is a huge improvement. We are seeing some of that where follow-up visits are farther apart because they are getting the data daily. If you weren't getting the data daily, then you would need to see patients more often to make sure that something isn't going bad," said PHT's Lee.

## Top Five Benefits of Electronic Health Records



Source: Assessing Adoption of Healthcare Information Technology, 2005, MGMA

## Top Five Barriers to Implementing Electronic Health Records



Source: Assessing Adoption of Healthcare Information Technology, 2005, MGMA

However, some industry experts express concerns about the ability of patients to handle the technology or processes necessary to assure reliable data if a clinical trial was conducted without a site and question whether the concept of a “patient-centered” trial even works.

“Clinical trials, by definition, are ‘patient-centered.’ The priorities of researchers and the challenges of data acquisition and analysis have led industry to forget that,” said Ronald Waife, president of Waife & Associates, a change management consultancy for clinical research. “Will yet more technology help alter the missing ‘patient-aware’ perspective, or will it lead to another long period of process adjustment with equivocal improvement? Since I believe that language is an important determinant of thought and behavior, I am concerned that ‘patient-centered’ doesn’t capture the issue. I think ‘real-life’ experience is what we are

after, because we fail, in controlled clinical designs of today, to actually learn what a therapy may or may not do, or enable, in patients in everyday life.”

### ■ Safety Concerns

As they re-examine how patients are engaged in clinical trials and how the process could be improved, drug sponsors must address regulatory questions that may arise and ensure the safety and protection of participating patients. “First and foremost, we need to be able to demonstrate that the patient is being properly monitored in terms of safety. The obligations of an investigator start from the moment of patient engagement around recruitment, screening and consent. We want to make sure that the patient is being appropriately informed throughout that

cycle and across the conduct of the trial,” Lipset said.

For all of its potential to reduce the time and cost of clinical research, while at the same time improving data quality, the patient-centered model raises questions about how patients, who are highly engaged and used to having a dialogue with their physicians, would feel about participating in a randomized, blinded clinical trial. “The nature of a blinded study is that we want the patient to be a little less informed,” Lipset said. “How do we keep that patient engaged and feeling fulfilled and satisfied in the study? What else are they getting in terms of a community or fulfillment out of participating in research that helps to make up for some of the decreased information they are going to be getting while they are participating in the study?”


To help make up for that lack of information during the study, Lipset

said drug sponsors could be more transparent with data and information with their clinical trial participants after the study closes. “Some patients may be fulfilled by increased engagement as a partner and contributor in the clinical process. We can also provide patients with summaries in lay language so they can understand what we learned from their participation. And we can provide their individual clinical data back through personal health records. This is a phenomenon that medical centers with their highly unstructured data have been able to resolve. We have clean monitored data sets, so we should be in a position to share some of that clinical information back with patients when the study ends, then they can decide how they want to use that information potentially to improve their own health in their relationship with their primary treating physicians,” Lipset said.

## Looking Ahead

Pfizer’s vision for a patient-centered clinical trial has far-reaching implications for how clinical trials could be conducted in the future. As technologies continue to evolve and drug sponsors have better and smarter ways to capture data from patients, using both telemedicine and self-tracking tools, there is potential for a significant change in the industry’s clinical development model. But, for now, Pfizer is taking the vision one step at a time.

“We have to take things incrementally right now and demonstrate that we can in fact engage patients in new ways and that we can potentially put existing tools together to enable more patient participation from outside of a clinic. Once we get to

that place, we can start to build and fertilize this ecosystem where other technologies and processes can be added and extend our ability to conduct such a trial in even more diverse patient populations,” Lipset said. 

—Karyn Korieth



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