SCRIP
CITELINE COMMERCIAL

03 Nov 2021 | **Analysis**

Industry Is Moving Fast With Decentralized Trials, But Is It Too Fast?

by Alaric DeArment

Companies like Bayer and AstraZeneca are seeing what a difference decentralization makes as CVS is rapidly expanding its clinical research business.

Industry has been quick to embrace decentralized trials as a lasting change, de-risked by the pandemic, and are reporting positive effects and cost savings. But during a recent panel at the Galien Foundation Forum, an important voice – former and possibly future US Food and Drug Administration commissioner Robert Califf – urged some caution about moving too fast.

During a 28 October panel discussion on how decentralized clinical trials (DCTs) are modernizing clinical research, industry experts reflected on the changes that have taken place to accommodate these new types of trials that use virtual and digital technologies and approaches. While it is now well established that the pandemic accelerated adoption of DCTs, there is still much to be worked out about how to incorporate new methods into the research system.

Medable CEO Michelle Longmire pointed out that DCTs are really opening up new possibilities, especially in rare diseases, due to their ability to ease participation in clinical trials, drawing on her experience at Stanford University doing research in the rare disease systemic sclerosis.

Decentralized Trials Ease Enrollment In Rare Disease Studies

By Alaric DeArment

“Here I am at Stanford, one of the few people really researching and treating patients with this condition, and in centralized care, we’re limiting that to the patients who live in that immediate area,” Longmire said. “So, there are important innovations, there are important treatment options, but it’s very limited in terms of who has access.”

SCRIP
CITELINE COMMERCIAL

While decentralized trials were embraced as a way to facilitate research during COVID-19, industry sponsors, researchers and regulators are seeing advantages – such as offering more flexibility in terms of sites and site visits to open up access – that are carrying the model past the pandemic to find a place in the clinical research landscape.

12 Aug 2021 Panel discussion illustrated how decentralized approaches can expand the possibilities of studies in rare diseases, such as cancers with rare genomic alterations. *Read the full article here*

Regulatory agencies have rushed to meet the growing interest in DCTs with guidance, accepting that fully virtual or hybrid trials are a permanent feature of clinical research. (Also see "*Sweden Tackles Regulatory Barriers To Decentralized Trials*" - Pink Sheet, 22 Oct, 2021.) The US FDA provided some instruction through its pandemic research policies and is working on a guidance on decentralized trials and use of digital health technology for remote data acquisition. (Also see "*Clinical Research Needs To Move 'Out Of The Ivory Tower,' FDA's Woodcock Urges*" - Pink Sheet, 7 Jul, 2021.) Sweden's medical products regulator is giving out free advice on DCTs to companies as part of an effort to investigate potential regulatory hurdles to their adoption. (Also see "*Sweden Tackles Regulatory Barriers To Decentralized Trials*" - Pink Sheet, 22 Oct, 2021.) And Switzerland's regulator, Swissmedic, which operates independently of the EMA, has issued a position paper on the topic. (Also see "*Switzerland Supports 'Increasingly Important' Decentralized Clinical Trials*" - Pink Sheet, 13 Sep, 2021.)

The research services industry has also been changing in response, with new players and new investment. Illustrating the growth in decentralized and hybrid trials, DCT technology provider *Science 37, Inc.* raised $235m in a merger with a special-purpose acquisition company (SPAC) and concurrent financing in early October. (Also see "*Science 37 Blockbuster SPAC Valuation Points To Growth In Decentralized Trials*" - In Vivo, 1 Jun, 2021.)

Panelist Andy Plump, president of research and development at *Takeda Pharmaceutical Co. Ltd.*, said that while the randomized controlled trial was "one of the great inventions, really, of the 20th century," the approach to it hasn't changed much and is "brutal" for physicians and scientists.

"It's inefficient, it's expensive, it's hard to find patients, and it's getting worse, getting more expensive and slower," he said.

But Califf, who is rumored to be the potential nominee for FDA commissioner once again, having served during the Obama administration, stressed the importance of sticking with the core fundamentals of randomized controlled trials, just with new technology. (Also see "*Potential For Califf's Second US FDA Commissioner Term Surprises, Excites Stakeholders*" - Pink Sheet, 14 Oct,

2021.)

DCTs Getting More Important In Research

Tony Clapsis, vice president for clinical trial services at *CVS Health Corp.*, noted that the company – which operates both the CVS retail pharmacy chain as well as the CVS Caremark pharmacy benefit management division – had sponsors ask for help setting up "really community-focused sites" to recruit patients for COVID and other trials.

During the pandemic, Clapsis said, the company engaged more than 1 million patients, and it expects that number to rise to about 10 million as it directly engages patients as well as opportunities for clinical research. CVS has opened about 15 community research sites, a number it expects to rise to around 40 by the end of 2021 and to probably about 150 in 2022. It launched the clinical trial services division in May.

"The idea is, how do you really cut that distance between home and site and provide a convenient community location for the patients to access research," he said.

For drug companies, that has translated into what amounts in many cases to a dramatic decline in the number of physical visits that patients have to make to trial sites.

"The way I look at it is, we started to actually bring trials to patients rather than bringing patients to trials, and that's a very fundamental shift," president of the Americas region for *Bayer AG* Sebastian Guth said, noting that in its trials, the company has seen drops in physical visits of up to 80%.

Meanwhile, *AstraZeneca plc* chief digital health officer for R&D Cristina Durán said that based on analysis of dozens of the company's own protocols, 70% of the data could be collected from home rather than at hospital sites, meaning that several protocols could be run as hybrid or even fully decentralized. The company has found it can reduce the number of visits to whatever is standard for the care of a given disease and significantly improve the patient experience.

"We have also seen that in programs where we can reduce the number of visits, it not only obviously helps the patient and sustainability for the planet to avoid all that traveling – it can also reduce the cost of the study," Durán said, adding that so far the company has found it can reduce costs by 20%-40% for some studies.

Tortoises Still Relevant As Hares Pull Ahead

As well as saving costs for sponsors, Longmire said the expansion of trial availability can aid patient trust.

"One of the biggest opportunities is to really get into communities and be a trusted partner," she

said. “Your trusted access points such as community pharmacies, such as treating physicians – I think we need to look at where those trust points exist.”

Decentralized trials also offer ways to get into different communities and draw in a more diverse pool of participants, particularly from populations underserved when sponsors concentrate studies at academic medical centers in affluent, urban areas. (Also see "*Will Decentralized Trials Continue Growing After COVID-19 Pandemic Ends?*" - Scrip, 17 May, 2021.) The greater flexibility around decentralized trials during the COVID-19 pandemic has been targeted as a way to improve health equity. (Also see "*COVID-Era Trial Flexibilities, Equity Focus, Could Be Used To Reshape Cancer Study Enrollment*" - Pink Sheet, 18 Jun, 2021.)

Califf, who now heads clinical policy and strategy for *Verily* and Google Health, emphasized that randomized controlled trials still remain crucial, especially amid the COVID-19 era with “all the ridiculous claims that have been made about drugs based on looking at databases.” He noted that not all people looking to make money on clinical trials are necessarily looking out for patients.

“And so somewhere in here, we have to strike a balance between telling the public that a clinical trial is a wonderful thing – which I believe it is when it’s well-done and proper – and the fact that there is a history of exploitation of people and research from which they need to be protected,” he said. “And I don’t think we’re at the right balance.”

Califf added that he likes the direction that things are moving, “but all of these things are reasons why the tortoises of the world need to still be in business, need to be looking at the hares and saying, ‘Wait a minute, maybe you’re going a little too fast. Maybe you need to stop and reflect on what you’re doing.’”

Longmire said that clinical research is ultimately about two factors – science and safety – but that speed is an important component as well, as long as it does not lead to a compromise on the other two factors. Califf agreed, but reiterated that emphasizing science and safety was still essential.

“I think the third variable should be speed, and when we don’t compromise the other two and we can also optimize for speed, there’s actually synergies you get from science and safety when taking speed into consideration and challenging the way we’re currently conducting the science,” Longmire said.