Highlights and Summary of Part 8 Webinar:

The Realities of Restart

wcg™

In the May 6 webinar, we turned our focus to the realities of restarting clinical trials. We begin by looking at WCG data spanning the clinical trials ecosystem, and then move to CEOs of two research sites to understand their challenges, concerns, and opportunities as they prepare to re-engage.

The panel featured:

1. **Suzanne Caruso**
   VP, Clinical Solutions, WCG

2. **Tom Wardle**
   CEO, Chief Executive Officer, CenExel Clinical Research

3. **Edward A. Jones, MBA,**
   President & CEO, Houston Methodist Research Institute

WCG Chief Medical Officer Lindsay McNair, MD, MPH, MSB, moderated.

This is the eighth in **a series of WCG webinars** that address the coronavirus-related challenges facing the clinical trial industry. You can find links to this webinar and an array of COVID-19 resources on our **WCG Insights Program page**.

The Post-COVID-19 Landscape

1 **Suzanne Caruso**
VP, Clinical Solutions, WCG

"I didn't think any of us really saw COVID coming. And it has really, really changed the landscape of clinical trials. One of the things I was thinking about is how much time I now spend on the Johns Hopkins website." People all over the world visit it daily to track COVID. This level of tracking is new, and the impact on clinical trials has been significant.

We have a disease and virus that basically didn't exist five months ago; now we have more than 950 active trials. Those are industry-sponsored trials, those are investigator-initiated trials. That's a lot of trials and a lot of patients that are needed in an incredibly short period of time.

COVID-driven Speed

COVID-19 forced speed, and that speed in getting trials ongoing is going to have a lasting impact on the clinical trial landscape beyond COVID.

In the past, conversations with sponsors would be along the lines of, "Well, can we get some real-time insights on what the enrollment rate is going to be in a particular therapeutic area? Can we look at the last two years?"

Now the conversation has changed. People who were starting clinical trials were looking at where to place their study based on the previous five days alone. That's how we're running trials now for COVID. The use of real-time information to inform trials moving forward will stick with us well past the COVID trial experiences.

And in talking about speed, we're seeing that most COVID trials are going from having a final protocol to first-patient first-visit in four weeks. Typically, this could be a six-month process. If you were really efficient, you might be able to get it down to three months. For COVID trials, this has now turned into a four-week process.

Agility

The industry has become agile as it has been looking for a treatment for COVID.

In an evaluation of about 40 industry-sponsored trials that were ongoing and active as of March 30, about 21% of the products were immune mediators, about 25% were antivirals. In just two months, there has been a dramatic shift to about 35% of the trials being immune mediators and 24% being antivirals.

Why does this matter? It relates to taking real-time information and changing strategy to inform where we think the disease, and COVID specifically, is going, something I think is going to last well beyond our COVID experience and that will be built into development of trials moving forward.

Beyond COVID-19

What about trials that were ongoing? What about trials in which we're enrolling patients? What has happened to those trials?

New, non-COVID-19 enrollment has slowed significantly, and trial holds have increased. Roughly 129 studies were put on official hold in April. The average number going into 2020 was about seven trials per month put on hold.

This is going to have tremendous impact as we come out of the COVID kind of clinical trial landscape and turn to newer or ongoing studies.

Those trials don't just disappear, right?

Meanwhile, as trial starts have declined, trials waiting to start have increased significantly. What does that mean? It means that we have a collision of forces with a number of trials that are ongoing and due to be reopened to enrollment with a number of trials that are getting ready to start and also going to be open to enrollment.

So, what do we do when we have this collision of new trials with restarts for studies that have been delayed as a result of that pause in enrollment?

In a survey conducted around April 25, we asked more than 1,250 sites across 29 countries, "How long do you think it's going to be before your specific site opens to enrollment again, and restarts clinical trials as they were prior to COVID?" About 37% said they're weren't sure, and 26% said, "Around four to eight weeks, we expect for things to start again on non-COVID trials."

Then, we asked the same question around May 2. Fifty-one percent of sites across these 29 different countries indicated they are going to be open to enrollment and new study starts within two to four weeks.

Looking Ahead: Questions Abound

We have studies that are on hold that are about to be restarted. We have new studies on the horizon. How do we plan for site resources to be able to support that and the competitive nature of getting those studies that are new studies at those sites, and who's going to have time to be able to take on those trials?

How are we going to plan for all of these individual forces that are coming together? We have a backlog of trials, and there are more active trials on COVID on the way. And with the sites that are going to be ready to restart, what does that look like?

Will they restart with only the studies that are already active but paused, on hold, or will they actually take on new studies? And will there be a triage into the types of studies they can take on? And how will sponsors adjust their trials in the same way that we adjusted during the time of COVID to respond to what the site says they can do?

Restart in the Age of COVID-19 From the Private Investigational Site Perspective

2

Tom Wardle
CEO, Chief Executive Officer,
CenExel Clinical Research

All of us at the site level, whether it's an academic institution or private investigational site, have been very focused on what we're doing to try to prepare ourselves and to assure our partners (CROs, sponsors, etc.) we are ready to restart enrollment or to start new studies that have been postponed.

Education and Information

Adapting to what's happening currently in the world requires strong educational response to study participants. In particular, it's important to demonstrate the ways the site is minimizing risk for participants and professionals alike--while maintaining the validity of the clinical trial data.

- **Educate the study participants early and often**
  - At pre-screen telephone interviews
  - At every facility entry/visit
  - At enrollment
  - Continuous reminders on use of PPE, social

Minimize the Risk of Infection at the Site

To minimize infection risk, sites need:

- **Pandemic-specific SOPs:** Development of formal, pandemic-specific standard operating procedures or working practices that are pandemic specific, including use of PPE, procedures for entering facility, testing procedures, etc. At CenExel sites, for instance, no one gets through the front door of the clinical research unit without being screened.

- **Remote monitoring procedures:** This is distinct from remote visits. It's incumbent on us to stay in regular contact with patients between outpatient visits and, while they're on inpatient units, to monitor them to ensure they're not exhibiting any symptoms and that they're following all the guidelines on PPE, social distancing, etc.

- **Remote visit procedures:** When applicable, sites should develop detailed study-specific plans (following FDA and IRB guidance) for remote visits of patients.

- **Follow current CDC infection control guidelines** for screening and implement necessary and reasonable precautions. Note that these guidelines change frequently.

- **PCR testing policies and procedures:** Determine when and how to test for active COVID-19 infection

(vs. antibody testing). Is it at screening? Outpatient visits? Inpatient unit entry? How often do you do it? Who pays for it? Is it incorporated into a protocol? It must be specific to the type of research unit that you have and where it's located.

- **Make site-specific changes in day-to-day activities.**
  - Reduce number of participants and staff in specific areas.
  - Schedule subjects throughout the day to avoid any high-traffic times. (This takes advance planning.)
  - Strictly limit access to facility.
  - Put in place plans and designate space to sequester symptomatic patients immediately.
  - Screen all staff daily at entry.
  - Follow all infection control and facility cleaning guidelines.

It's critical that you demonstrate to patients you're taking these things seriously. That's going to allow us to be able to restart and continue to enroll patients as safely as we possibly can, to minimize the risk as the industry starts to reopen enrollment for clinical trials.

The Realities of Restart

3 **Edward A. Jones, MBA,**
President & CEO,
Houston Methodist Research Institute

Echoing the previous comment: The safety of our participants in the environment is essential if we want to continue what we're doing.

The Houston Methodist Perspective

We didn't shut down many of our operations. I wanted to give a context of Houston Methodist and why we made those decisions, and some of the things that we put in place throughout the COVID crisis that have positioned ourselves as we moved towards the new normal for patient interaction and for clinical research.

We have nearly 300 front doors in the Houston Methodist System scattered throughout the greater Houston metropolitan arena. That becomes important because, as we're thinking about our clinical research, COVID has put pressure on us to stand up new protocols within weeks. Some of those have been pushed out into environments that have not traditionally had clinical research, some of those into our community hospital settings–many of those looking to network our primary care settings.

Houston Methodist has an academic medical center, six community hospitals, and a long-term acute-care facility. That acute-care facility became pivotal throughout the COVID crisis: It was converted to an infectious disease unit. That will remain in place and will give us a new opportunity for clinical research moving forward.

Because Houston is a very active hurricane area, a very wet area, Houston Methodist already had a robust incident command. By having a structure in place, we were able to be among the first to be able to stand up for remdesivir as a clinical trial option for our patients with severe respiratory distress. We also were among the first in the country to stand up plasma convalescence.

To do that, you have to have the expertise, you have to have the structure. And from my vantage point, you kind of got to get out of the way a little bit and let smart people figure this out. And they did an incredible job of that.

Reopening: The employee perspective

Key considerations:

- **Fatigue and fear:** The staff have been through a lot. They are exhausted and overwhelmed. They are trying to make sense of the coronavirus-related news, and many are fearful.
- **Local, state, and federal politics:** It's not a partisan

statement to say these are often not aligned. And so a local mayor or county judge says something that may contradict what a governor is saying. We have to sort through that, make sure we bring the staff back not just in a regulatory-compliant way, but also keeping in mind not just what a governor's order is but what the local community expectations are that may not be legislated.

- **Testing and surveillance:** While PCR testing for active COVID infection is highly reliable, many other tests may not be.
- **Staffing levels**
- **Dependent care:** Some employees caring for children and parents may not be able to come back. And some may be in quarantine.
- **Social distancing**
- **PPE:** Do you have adequate PPE? Houston Methodist has 25,000 employees. For us to give to give two masks to every employee, that's 50,000 masks and that's what we're able to do. But when we go into monitors, we go into visitors, we go into other people that need to interact with our healthcare system, we can't provide PPE for all of those. We need to be able to communicate that.
- **Cross-functional resources:** As we headed into the crisis, we did not have an infectious disease presence in clinical research that was adequate to handle all of this. We had to move and migrate coordinators and study personnel from different operating units into COVID-19 trials. Well, now as we look to stand those back up, we haven't found a whole bunch of new coordinators that we can hire and bring in. So how do we balance the ongoing need for this new line of inquiry that desperately needs to be resolved with returning people into their normal operating units?

Sponsor considerations:

Obviously, we're not the sponsor, but things that the sponsor organizations and site organizations need to kind of talk through are:

- **Flexibility:** Standing up 950 trials within weeks demands flexibility on both sides.
- **COVID-19 competition**
- **Local IRB vs. Central IRB:** We've seen a nicely balanced interaction between central and local IRBs.
- **Contract and financial terms:** The contract and financial terms aren't what they were and quite frankly, neither is our patient population. Moreover, health systems are in dire financial straits. Every 1,000 beds of a healthcare system represent about a $100 million dollar loss and you can extrapolate up or down from there.
- **Fewer patients:** People are likely staying home because they don't want to return to the healthcare arena. That's a problem.

Questions from Audience

1 **Suzanne Caruso**
VP, Clinical Solutions, WCG

2 **Tom Wardle**
CEO, Chief Executive Officer, CenExel Clinical Research

3 **Edward A. Jones, MBA,**
President & CEO, Houston Methodist Research Institute

Q **Suzanne, you talked about seeing activities towards new study preparation. Are there certain therapeutic areas in which you're seeing more activity than other therapeutic areas?**

A **Caruso:** I think oncology is where we have seen a bit of activity and there's more ready to go in June, July and August in that space. I would say it's actually mixed between big pharma and small biotech.

One of the things I didn't mention is that the landscape for big pharma and small biotechs is really different in that you can have a huge portfolio of oncology trials where you might be able to pick if you're a Novartis, that you can choose, "Okay, I want to prioritize these five." Some of the smaller biotechs might have two studies that they need to get started immediately. So, the pressures are coming on both sides as well. But to specifically answer your question, it's definitely oncology.

Q **Tom, you talked about screening staff and screening people as they come into the clinic setting. We had this one question that came in asking what's the extent of that screening? Are you talking about screening for symptoms, temperature screening? Are you talking about actual PCR viral test? What does that screening entail?**

A **Wardle:** Again, it needs to be tailored a little bit to your specific institution. But I'll tell you by way of example what we do.

When employees come in to our units–and I'll use myself as an example–I'm stopped at a sequestered area by employees that will make me wash my hands or sanitize my hands, they'll remind me on the use of PPE, they'll take my temperature.

And then there are the containment questions: Any contact or exposure? Flu-like symptoms? Where have you traveled?

Now the question about testing is one we'll need to probably spend half a day on, and it gets complicated. For employees I'm specifically referring to, we are not testing employees. The reason for that is, as I said, it's very complicated.

I'd like to kind of mention and discuss just briefly a framework around testing. Whether it's for patients or participants, here are the things that you have to think about. First is, what type of a test are you doing? Is it an antibody test? We know that, and I've heard the term used recently, it's the wild west of antibody testing right now. The FDA just the other day released guidelines on emergency use applications. There are a lot of bad products out there floating around right now. Some very good ones, too, but even if you do antibody testing, what does it really tell you about recent infection, long-term infection, current infection, all sorts of downstream questions that have to be answered there.

How often do you do it? Just because you have a negative PCR test today doesn't mean you're going to have one tomorrow or next week. If you have a lot of employees coming out of your clinic, that would get very expensive very quickly to do PCR testing, even if you could get rapid turnaround on those tests.

Generally speaking, it's not rapid turnaround at this point, with some exceptions. I think we'll see more productivity and doing a quicker, more rapid turnaround for antigen or PCR testing in the near future.

The bottom line for us is for patients, yes we are, as they come into studies, are coming into clinic, doing PCR testing, but not for employees at this point. And we'll just have to evaluate that situation as we progress down the next few weeks.

And reporting requirements vary from locale to locale, state to state, etc. And you have to think very carefully about what those reporting requirements are, what they mean, the implications for those long term. Our goal still is to try to be as safe as we possibly can, but there's a whole host of issues around reporting requirements that you should think about as well.

Q **Ed, we're talking about restart, but at the same time, there are concerns about either a second wave of infections later this year or a continuation of the number of infections, and some plateauing. So, what is the thinking about a slow start to reopening sites and then a second wave of cases that may shut things down again?**

A **Jones:** So first, I think COVID is with us for a while. I think almost assuredly we're going to see an uptick as people begin to emerge from their houses. I just don't see how it's not going to happen. Having said that, I do hope that we're able to avoid the overwhelming pandemic levels that we were really worried about seeing. And luckily, we saw drastically increased levels in Houston, but not ones that overwhelmed our healthcare delivery systems. So, I think we're going to see a range between where we are now and, I'm hoping, mildly uncomfortable ranges of COVID-19 infections. I think as you're looking to open, I think you have to look towards that and opening up in a reality that COVID is going to sort of mediate between the background and the foreground for the foreseeable future. I don't think we can open and say, "This thing is over," by any means. And so, as you open, I think you have to open in ways that assume that there's still a high prevalence of COVID-19 community transmission and take those safeguards.

Again, many of which Tom described in detail: social distancing, spreading your staff out, testing, keeping logs of employees, looking at travel. There's going to be all these myriad indications that as sites open, they're going to have to stand up. And what I would say is stand up as though you were going to continue to operate in the presence of COVID-19. Because I think to do otherwise is just shortsighted. We see those uptakes in the coming weeks as we relax the stay-at-home orders, or we see it in the fall because there's some seasonality to the infection.

Q **Suzanne, from a site perspective, what can sponsors be doing to support sites in their ability to restart research?**

A **Caruso:** To be succinct: Help study coordinators. I do not think there's a bigger impact that sponsors can make than to supply support to study coordinators. Think about the things that we're talking about. Like collision of course, studies on hold and studies in planning and the largest therapeutic area that has the most pressure to start studies being oncology. There are more requirements in data entry in oncology than almost any other therapeutic area. There's going to be tremendous impact in the amount of resources that their study coordinators have to cover both for their new studies as well as for COVID work that's still ongoing.

That study didn't end overnight. There are going to be COVID trials for a number of months if not years moving forward with the vaccine trial. So, providing clinical research coordinators for a study to be able to do data entry, to be able to do scheduling of patients and keeping track, I think is the best way to support our site colleagues. And that's something that I think a lot of sponsors are looking into. In addition to remote assessments and remote visits. So that's my take on that question and I think the more support we can give those coordinators, the better we'll feel kind of coming out of this.