
# Highlights and Summary of Part 10 Webinar:

## Unique Challenges and Opportunities for Emerging Biopharma Companies with Focused Pipelines

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## The panel featured:

1. **Michael F. Cioffi**
   *Senior Vice President, Clinical Solutions and Strategic Partnerships, WCG*

2. **Manny Lazaro, MS**
   *Vice President, Head of Clinical Operations and Data Management at Jounce Therapeutics, Inc.*

3. **Omer Siddiqui, MS**
   *Vice President, Development Operations at Alector*

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

This is the 10th 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 Shifting Marketplace

**1** **Michael F. Cioffi**
*Senior Vice President, Clinical Solutions and Strategic Partnerships, WCG*

WCG's Michael Cioffi set the stage, providing a glimpse of what's happening in emerging pharma compared to their mid-size and large pharma counterparts.

- **Study starts in 2019:** Emerging pharma study starts outpaced mid to large pharma study starts in 2019. Data from the WCG Knowledge Base™ shows there were over 40% more interventional trials started by emerging pharma. That trend is continuing in 2020. (We define "emerging pharma" as companies with five or fewer study starts.)

- **Percent of studies on hold in 2020:** In the age of COVID, we've seen a lot of studies go on hold. Emerging pharma companies have started more trials and put fewer on hold. Emerging pharma started more trials in 2019, but only 43% of their trials have been placed on hold since COVID-19, compared to 57% of mid-large pharma.

These findings reveal a difference in the mindset and the mentality of the emerging pharma companies, emerging biotech, versus the mid-to-large pharma companies. This is an exciting shift in the marketplace.

# A 3 Phased Approach to Handling Clinical Trials in the COVID-19 Era

**2**

**Manny Lazaro, MS**
*Vice President, Head of Clinical Operations and Data Management at Jounce Therapeutics, Inc.*

Jounce Therapeutics is a clinical-stage immunotherapy company in Cambridge, Mass., dedicated to transforming the treatment of cancer. "We're discovering and developing novel cancer immunotherapies designed to harness the immune system, to attack tumors, and provide long lasting benefits to patients."

The company is about eight years old; the clinical development organization started in 2016, at the time when our first compound entered clinical studies. It currently has two clinical-stage programs. First, vopratelimab, a monoclonal antibody that binds to and activates ICOS, which stands for inducible co-stimulator; and JTX-4014, a PD-1 inhibitor intended for combination use with Jounce's broader pipeline.

Oncology, at most of its institutions, is considered a priority disease area. "Therefore, and so far, knock on wood, the impact of the COVID-19 pandemic has been modest in nature, due to some very creative mitigation steps implemented by our team and service providers."

## Jounce Timeline

Lazaro identified three phases to the company's response to COVID-19. The Acute Response phase lasted about two weeks, from mid-March to the beginning of April. The Adaptive Implementation phase lasted from early April through mid-May. The third, which they're entering now, is Recovery-Road to the "New Norm."

## Phase One: Acute Response

There wasn't much time to respond and put mitigation strategies in place. "I'm so proud of our team at Jounce for not panicking and swiftly developing mitigation strategies, along with our service providers, while maintaining a positive spirit."

- **Keep ongoing studies open:** The approach was to keep ongoing studies open to enrollment and follow up, taking the lead from clinical sites. This required

remaining flexible and adapting to the clinical site's situation and local guidelines: "One size does not fit all."

- **Perform a risk assessment and impact analysis.** Jounce tracked the following areas and then assigned a potential impact on the trial:
    - Participant safety
    - Enrollment
    - Monitoring
    - Sponsor oversight
    - Central lab and specialty labs
    - Service providers
    - Participant follow-up and visits
    - Investigational Product
    - Data/study integrity
    - Internal resources

The end of phase one involved developing mitigation strategies to keep the operation moving and enhanced site communication. It was essential to remain in close contact and communication with our clinical sites. That included implementing routine study coordinator calls, not only to obtain feedback, but also to hear and learn about the challenges they faced. Jounce already had in place medical science liaisons to help with our site management and study engagement.

## Phase Two: Adaptive Implementation

With the rapidly changing environment, the mitigation steps we put in place last week may no longer be relevant today.

- **Ongoing close communication with the clinical sites:** Overcommunicate. The sites have the lead trial manager's and the medical director's personal cell phone numbers so they could rapidly get answers to their questions, whether it be around eligibility, protocol, procedures, enrollment strategies, how to handle protocol deviations, drug administration, missed procedures and visits, and the consent process. The sites really appreciate this in real time and having access to us. "Because of this frequent contact with our sites, I think my team now knows the names of all of our PIs' children and their pets."

- **Prioritized study-level workload:** One area where we paused activities was around the resolution of data discrepancies. These were deprioritized to allow the site staff to spend more time on the more important activities of the trial in situations where time was either limited or staff resources were reduced. There'll be an opportunity to catch up on some of these later when things return to normal.

- **Remote audio/video monitoring:** "I believe we've maintained our effectiveness and quality, especially for those sites that allow external access to the EMR systems." If this wasn't possible, sites were asked to send redacted health records to a secure portal or send via a password-protected email. However, this solution is very burdensome to the site staff. If neither of these solutions was possible, then the CRA would conduct a teleconference with the investigators or coordinators following a checklist of questions focused on patient safety.

- **Remote training:** One requirement before a site could be activated was that the site had to independently demonstrate proficiency in the processing after the training. So, in a remote setting, the newest sites are capturing their technique via video so we, as the sponsor, can assess their technique. We also created a training video with all the steps outlined, and the sites really like this, and are now asking for more trainings using this format.

- **Support for site staff shortage:** In a handful of situations due to a reduction of staff resources, we've provided coordinator support through WCG ThreeWire. This temporary support could help with data entry, patient improvement and other study coordinator duties. Fortunately, we had this in place pre COVID, so we could rapidly deploy the support when requested.

## Phase Three: Recovery - The Road to the New Norm

Moving into the recovery phase we (at Jounce) fully understand that things won't be done the same way as they were, say, prior to March 2020. Among the approaches to this new normal:

- **Support for clinical research staff** with backlogs and other issues.

- **Doubling onsite CRA support** where needed.

- **Continuing to monitor the impact on the data integrity.** Jounce is providing real time information to assess the impact, if any, and whether any study-level changes need to be made.

- **Focusing on documentation:** At the end of the trial we want to ensure we can recreate an accurate story in our trial master file, but also describe the steps and the actions we've taken due to the COVID-19 and the CSR. Time will tell as to whether we handle this situation adequately, once we obtain inspection reports from the regulators and our QA colleagues post COVID-19.

## Future Possibilities in Clinical Research

This pandemic may provide the impetus to modify and change some of the ways we have traditionally conducted our work. It may also provide companies and individuals in those companies with the comfort and confidence to adopt new technology or more efficient, less-resource-consuming approaches, such as telemedicine, sending business to remote monitoring.

We're fortunately in an era where science is moving at a rapid pace, which is fantastic for patients. However, the clinical research industry has to find ways to be more efficient, in order to keep pace with these advances in science and technology.

Telehealth has made strides. Here's just a sampling of some of the innovative solutions that have been deployed.

**Enabling technology**, including wearables, real-time big-data analytics and visualization, e-consent, ePRO and eCOA, AI and virtual trials.

**Remote monitoring and risk-based monitoring:** Assuming that overall compliance and data integrity are not compromised, "this is an area we should aggressively implement into the post COVID-19 era, as a standard, in my opinion."

**Flexible protocols** that include provisions to enable mitigation steps in the event of another health crisis, or even a natural disaster. By incorporating these provisions, we could avoid amendments and protocol deviations.

**Improved communication and collaborations:** This has improved during the crisis; it should continue. Why does it take a pandemic to bring us closer together? "We need to unite as an industry to create new standards, essentially jump into the pool with both feet."

**Clinical trial continuity plans:** Most of us have business continuity plans. Should we develop continuity plans specific to how we handle situations like COVID-19 in the future, so we're better prepared?

## A Pre and Post-COVID World: Can Things Ever Be the Same?

**3** **Omer Siddiqui, MS**
*Vice President, Development Operations at Alector*

Alector is a bio-pharmaceutical company in the South San Francisco Bay Area with a focus on neurodegeneration--harnessing the brain's immune system to tackle these diseases. "We have a deep neuroscience expertise, from research to manufacturing, to the clinical side of things. We're combining the expertise with genetics to target this immune dysfunction." It has four programs in the clinic.

### Defining Our Terms: Remote

When we talk about remote options, we use the terms remote assessments, remote monitoring and virtual trials; in many cases, I think a clarification has to be made.

- **Remote assessments:** Conducting assessments outside of an actual in-person site visit, typically from the patient's home.

- **Remote monitoring:** Online review and validation of data entered in electronic databases, site interactions, etc. Fewer on-site visits by clinical monitors.

- **Virtual trials**, both fully virtual and hybrid approaches. No physical site or direct in-person contact. We hear about big trials that are virtual, using devices. That gets tricky in the neuroscience space. In Alzheimer's or certain types of dementia, we can't really get away from patients coming in and seeing these specialist neurologists. Yes, we can leverage some tools, electronic tools--we're actually working right now with WCG to be able to conduct some remote assessments. But in our patient population, we take the hybrid approach.

## Main Areas of Impact

Where did the pandemic have the biggest impact on Alector's trials?

- **Patient screening and enrollment:** Depending on location, site staff were reassigned to COVID activities; sites were limited to essential research--which often doesn't include new patient screening and enrollment.

- **Less data available for decision-making** because of missed study visits.

- **Disruption in sample testing:** For our trials in the neurodegenerative space, it's not just a clinical outcome assessment that we're doing. There are MRIs, PET imaging happening, multiple labs, lumbar punctures, etc. It truly takes something bigger than a village to conduct even one small neuroscience trial.

- **Extending timelines due to enrollment disruption**
  - Delays finding treatment for patients
  - Leads to extended engagements with CRO and vendor and higher budgets

- **Maintaining site engagement:** Sites need to know they have sponsor support.

## Key Focus Areas as Clinical Research Sites Reopen

**As sites reopen, where is the company putting its focus?**

- **Managing the informed consent process:** We limit the in-person travel that has to happen. We're providing a lot of patient, caregiver, family education.

- **Patient and caregiver education:** For example, drug self-administration can be a pretty tricky thing. When you're dealing with subcutaneous injections or, in our cases, for example, when you have IV drugs, that

gets very tricky. Even having home care nurses to do or doing at-home infusion, there's a lot of nuances to it you have to watch out for. Training on patient-reported outcome instruments is also important.

- **Collection of the adverse events:** In some situations, you could do it remotely. But in others, especially related to dementia, you can't. Often, you have to have the patient plus the caregiver with an investigator, with a trained rater to conduct these.

## Prioritizing Efforts: Where's the Greatest Value for Investment?

We have to prioritize our efforts. A lot of ideas--great ideas--get thrown around. But you need to identify what the biggest impact would be for the least amount of investment that we can make at this point. Among the questions to ask:

**On the investment side**

- How much time does it take to implement?
- How much does it cost?
- How much variability does it add to the measure?

**On the impact side**

- Can it apply to multiple programs?
- How likely is it to reduce missing data?
- Are there regional constraints?

Even though one blanket umbrella approach doesn't work, we have to see how we can consistently do this across our studies and how likely it is we can mitigate the missing data or the missing assessors. And then, there are a lot of regional constraints, right? Every country, every regulation is different.

## COVID: Before and After

"Can things ever be the same as they were before? I think not." But some things are constant:

- Patient safety remains the primary focus
- Regulatory agencies need to keep up with the ever-changing situation
- Reduced site and patient burden with hybrid approach to protocol assessments
- Use of telemedicine, home nurses, direct-to-patient delivery of study drug
- Patients'/caregivers' experience and knowledge of clinical trials

"Everything is a learning in life. Yes, what happened, happened. How can we come out better from this in what we can apply to our work, to our world of clinical trials and clinical drug development? I'm sure, at the end of the day, it's always patients at the end of this line."

## Questions from Audience

**1** **Michael F. Cioffi**
*Senior Vice President, Clinical Solutions and Strategic Partnerships, WCG*

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**Q** **Mike, you showed some data from 2019 and the proportion of study starts that were coming from companies that were small and emerging biopharma. If we had looked at that same data a few years before, it would have showed us that the majority of studies, more than 60%, were actually coming from mid- to large-sized biopharma, so that's a pretty dramatic shift over a fairly short period of time. Why do you think we saw that shift? What changes or trends in the clinical research world do you think that change reflects?**

**A** **Cioffi:** I'll address one topic in there and I think it's the move to rare disease. You've seen a dramatic shift in the amount of work we see now in rare diseases. And a lot of times, it's the smaller biotech companies that are really specializing in some of these areas and really driving the research and development that we see in rare disease.

Another part of it is looking at the populations which we try to treat. Historically, if you go back 10, 15 years and you see the way in which pharma would develop a drug, they would just pick an indication and treat anybody and everybody with that indication. And now you see our trial design being a little more savvy where we look to enriched populations in our trial design. And I think, again, that is better suited for the biotechs and the emerging biopharma to take on than we see with large pharma.

**Q** **Manny, you mentioned when you started to do your initial kind of risk assessment and impact assessment that participant safety was at the top of your list and your first consideration in this risk and impact analysis. And I know that's something that we've talked about a lot and something that gets talked about a lot when we consider the idea of virtual trials or hybrid trials and using telemedicine to replace in-patient visits. How did you kind of make that assessment? We talk about whether it's okay to do a visit by phone; otherwise, if that patient had come in, they would have had their vitals checked and they would have had a physical exam done. How did you assess whether it was okay to make those changes? What kind of considerations did you make around that?**

**A** **Lazaro:** It wasn't one size that fits all, so we really needed to understand the capabilities or reduced capabilities at each site. But overall, I would say from a safety perspective that we didn't see our safety assessments compromise people. Our patients still came in for their IV administration. I neglected to mention that, but our drugs are administered by IV, so we didn't miss any of those. There were cases where some institutions didn't allow blood draw-only visits. In those cases, we do use local labs. We allowed patients to go to their local laboratory in order to get their safety labs and then those were sent to the investigator.

And then, with regard to our sites, just having more frequent conversations with the patients--not just asking open-ended questions, but being more targeted about what may be happening with them from a safety perspective.

Overall, I think we've gotten through this period of time without much compromise on our safety. We did look at a home health nurse care and also home IV, but we didn't have that in place. And this goes back to what I said earlier. Should we plan for this so that we can deploy it when needed? So, as mitigation, we talked to a number of vendors. We know there are a number of vendors who provide the service, but everybody else in the world was calling them too. And the lead time to get these in place

was eight to 12 weeks, and that certainly wasn't going to help us in the immediate future. So we abandoned that because, again, our sites have been phenomenal and have been maintaining the study visits and their safety oversight.

**Q** **Omer, one of the things that you mentioned was participant and caregiver training around things like study drug administration and things that they can do at home as part of a study. What tools or methods have you found to be useful to do that, to train participants or to give them education about study components?**

**A** **Siddiqui:** We haven't done that for a lot of our patients, a lot of our sites. In fact, actually because these patients have no other treatment option--and in some cases no trial options--the hospitals and the PIs made arrangements to have the patient come in for their IV infusion.

There are some basic dose administrations that happen but the key thing for us is that for IV infusion, there are home care nurses or satellite centers that are close to the patient that they could go to. So that's what we've been exploring as an option of reducing the time that it takes.

IV infusion can take anywhere from a half hour to an hour or more, plus the travel times to sites, we're trying to reduce that by looking at options for home care nursing visits to happen. They're qualified and trained in making sure the appropriate methods are taken to protect the patient and themselves from any of the infections to pass on. So that's what we're looking at right now.

**Q** **Manny, one of the things that you mentioned was that you, as the sponsor, have been trying to provide some additional support to research staff during this time. Can you tell us a little bit more about how you're providing that kind of support to the staff?**

**A** **Lazaro:** We were already planning this pre-COVID. We know often sites are short staffed and they often take on more studies than they're capable of doing and satisfying all the demands by sponsors and CROs.

So we built in from the beginning, as I mentioned in my presentation, the study coordinator support

from WCG ThreeWire. And right from the beginning we offered this to every single site. Some sites' institutional policies don't allow contract or temporary help to come in. But for those sites that could, we were providing that support and we were paying for it because we knew we wanted the sites to have adequate staffing in order to conduct a trial.

We saw a little bit of uptick when COVID-19 hit us. And we've been getting those requests and because we already had the contracts in place where we had the systems processes in place, then we were able to deploy that upon request.

And as I mentioned, we are in close communication with the sites. So we've gotten requests to revise budgets, to allow for remote monitoring. We've gotten requests for ID supplies because the hospitals were running into shortages of some of the ID supplies, PPE and so forth. So we were really listening to the sites and their feedback and trying to support them in every way we could.

**Q** **Omer, from your perspective, what could sites be doing that would be really helpful for you? What could they do or--or not do--that would help sponsors in a way that would ultimately provide the best outcome for both the sponsors and the sites?**

**A** **Siddiqui:** That's an interesting thought and a nice way to look at it. It's always what the sponsors can do, what the CRO can do to support sites, and what you always hear is "don't bug them."

But, my perspective on this is, we are going to these qualified investigators for a reason. And that reason is, primarily, patient care. And I think to me, that's the foremost thing for us that the sites can do. They have that touchpoint-- they have that communication with the patient.

So, yes, I understand these are unprecedented, very difficult times for everybody, but we have to make sure that patient interaction is there. These are patients, sure they're research patients not everyday patients that are coming in, but their lives are impacted every day. So I think to me, what sites can do, site staff, not just investigators but research nurses, coordinators, they can make sure the support is there with the patients, however they do this. So FaceTime or video calls or just phone calls or emails. I think to me, that's the key. Everything else then becomes secondary in trying to ensure procedures are being done or those kinds of things are being done.

And everything else that comes secondarily. We can work together, as long as the lines of communication stay open.

**Q** **Manny, is there anything that you would add to that or that you would suggest?**

**A** **Lazaro:** I would answer that question by just asking the sites to be very bold and be very open and candid about what they need, or what we could do better. We do want to treat this as a partnership and not just someone or a team executing to a clinical protocol.

So, whether the protocol is too complicated or unclear, or whether we're emailing them too much, or we're asking them to do things under unreasonable timelines--whatever it may be, I think there are times when there needs to be some pushback. We really want to understand some limitations so we can approach the execution of these trials in a partnership.

Even as part of our trials, we conduct surveys and questionnaires, and we want to get feedback on how we're doing as a sponsor and how our service providers are doing too and where we could improve. So we truly look at it that way. So, like I said in my presentation, give us the feedback.

**Q** **Omer, you talked about the administration of your drug being IV and some of the procedures that have to happen in person. So clearly the staff that are working with the participants in your study can't follow physical distancing guidelines. Has the FDA released any guidance that suggests how, during clinical studies, precautions should be taken to manage those situations where physical distancing is not possible? How are you handling that in your study?**

**A** **Siddiqui:** I don't know if there's specifically an FDA guideline, but as you mentioned, there are CDC guidances on a lot of the procedures.

I think part of it is for some of these types of assessments, like PET imaging or MRI assessment. These facilities aren't just trial sites; they see other patients. I think they minimize the nonessential visits. Some made arrangements to do only one person coming in. No one is in the waiting room and the staff has the protective equipment and all of those procedures in place.

So yes, there's no social distancing, but when you're doing imaging, you're a little bit far apart when you're doing the scanning. So I think it's just minimizing the impact. Sometimes, it's rescheduled. If an imaging assessment is a few weeks or even a month away from what we originally anticipated or

planned for, the results are not that highly impacted just because what we were looking at isn't day-to-day--like bloodwork is.

So, it's kind of a mixed approach that keeps patient and site staff safety at mind.

**McNair:** From both the centers and the sponsors that we speak to often as well, I would say that seems to be pretty much the approach that everyone's taking. That if there are procedures that are part of a clinical trial that are also clinical-practice procedures, then the same precautions and steps that would be taken for those procedures being done in clinical practice would also apply to procedures being done for research. And while there may not be FDA guidance on this that is specific, people might want to check the CDC website. There are some guidances or guidelines on there for the protection of healthcare providers when they're providing healthcare.