EgonZehnder

Synthesis

"A Generation of Medicines at Risk"

Egon Zehnder Virtual Meeting: Biopharma R&D Executives

On April 25, Egon Zehnder virtually gathered heads of R&D from pharmaceutical and biotech companies to discuss the impact that the COVID-19 outbreak has had on research and development activities. Moderated by Elias Zerhouni, a Senior Advisor to Johns Hopkins Medicine and previously the President for Global R&D at Sanofi, Director of the NIH from 2002 to 2008, and a former Senior Fellow at the Bill and Melinda Gates Foundation, with assistance from Egon Zehnder partners Lee Wrubel and Joanne Yun, the two–hour conversation reviewed the current state of research activities, early and late clinical development, and interactions with regulatory agencies. The discussion included sharing best practices for operating R&D organizations during these difficult times as well as working with key partners including CROs, clinical trial sites, and academic collaborators.

Prior to the discussion, the R&D participant group responded to a survey in which they were asked which aspects of their work were most affected by the crisis. Topping the list was disruption to project timelines, in vitro and in vivo experiments, clinical trial site initiation, patient enrollment, and ongoing clinical study integrity. The range of topics discussed can be found below, organized by decreasing importance:

All Survey Topics in Descending Order of Disruption

How has the crisis impacted the following Research operations?

- Project timelines
- In vitro experiments and screening
- Work with collaborators and external partners
- Animal studies and vivarium operations
- Work with contract research organizations
- Business development discussions
- Chemistry and compound synthesis
- Partnerships with academic institutions
- GLP toxicology studies
- Structural biology

How has the crisis impacted the following Early Development operations?

- Patient enrollment
- Initiation of Phase I studies
- Clinical pharmacology
- Project timelines
- Biomarker samples
- IND enabling studies
- Work with collaborators and external partners
- Business development discussions
- Regulatory interactions, including End of Phase II studies
- IND filings
- Clinical supply
- Engagement of Key Opinion Leaders
- Data management
- GMP logistics

How has the crisis impacted the following Late Development operations?

- Initiation of Clinical Studies
- Patient enrollment
- Project timelines
- Clinical monitoring
- Patient compliance
- Work with collaborators and external partners
- NDA filings
- Medical affairs
- Regulatory interactions
- FDA Advisory Committees
- Data integrity
- Protocol amendments
- Clinical research
- Clinical supply

The conversation addressed these topics, with several major themes emerging.

The choice to stop or continue ongoing research activities

Companies not working directly on COVID-19 related projects have had to make a painful choice: whether to stay open, perhaps risking the safety of their workers, or to close, which means losing precious momentum and ongoing experiments. Early stage biotechs with an imperative to demonstrate pre–clinical results to investors are demonstrating that research activities can be safely pursued with appropriate social distancing. One R&D leader of a pharma company who also serves as a director of a small biotech stated, "We [in pharma] have the luxury of supporting our colleagues during this time by keeping them at home. But a small [company] does not – the clock keeps ticking every day. And they don't have money to continue that. So are we being too conservative or are the biotechs being by necessity too aggressive? I struggle with that dilemma."

Small company executives echoed that continuing operations was in many cases a matter of survival. They shared how they are keeping their workers safe; ranging from enforcing social distancing to creating shifts in the lab to reduce density to, in one case, paying for employees to take Ubers to work so that they could avoid public transportation. "They just don't have a choice," one board member said. "They're facing real funding crises, and they have to make their deadlines." The new rules seem to be working and energizing, said the head of R&D of a pre-IPO company. "Our employees have been incredibly willing to come in. It's actually been really heartening to see, and many of them have wanted to do R&D research focused projects on coronavirus in their spare time in the lab. And so they've been brainstorming on their own about how they can do this." However, many executives commented that certain highly specialized activities, such as flow cytometry, do not yield themselves to social distancing, suggesting limits to these approaches, at least for the moment.

Demands on employees who are parents or who have other complicated circumstances is another issue companies are trying to solve. As one pharma executive said: "Certainly, one of the priority activities has been identifying those that need to stay at home to take care of their children, with other colleagues stepping up to solve that." Another executive mentioned that his organization has kept its onsite day care running.

But even where labs and factories are beginning to reopen, in Asia and elsewhere, executives say they are trying to be respectful of employees' personal timetables. "If some people are just scared to come in, we're not going to make them," says one. Another wondered where you draw the line. "It's really a difficult tightrope to walk you obviously don't want to force employees to come in. But the range from you know, rational fear to irrational fear is pretty large. So if this continues all the way through the fall, it almost crosses over into performance questions, especially in a small biotech." Interestingly, the R&D participants noted that business development activities continue to progress without much negative impact so far, and scheduling for business development discussions is significantly easier due to work from home mandates and travel restrictions.

The criticality of salvaging clinical trials

The biggest challenge for biopharma companies—and for patients—is the disruption that the crisis has caused to existing clinical trials across therapeutic areas. While many early-stage trials have been abandoned or postponed, others have continued nearly on schedule. Enterprising leaders have found ways to virtually initiate new clinical sites around the world, including in Italy as the country recovers from its COVID-19 shutdown. Regulatory responsiveness has been better than anticipated; the FDA, for example, was praised for largely achieving its goals of a one-to-three day turnaround for IND reviews of COVID-19 related programs. One executive stated, "I know from personal contacts at the FDA that people are working through the night and through weekends in order to make those approvals happen."

Many trials—particularly late stage trials, which make up 50% of industry's R&D spending are at risk of failed outcomes as trial sites are no longer available for clinical assessment, while patients may be lost to follow up. COVID-19 infection as a variable influencing outcomes is also a significant potential issue. The risks to data integrity are profound and require careful quantified assessment and mitigation. These problems are magnified because industry sponsors must collaborate with external parties such as CROs and academic centers regarding clinical site stability and clinical operations. Working proactively with partners and regulators to manage studies proactively and creatively, including such strategies as adaptive trial designs, Bayesian statistical analyses, or increasing patient sample size should be carefully considered.

Says one senior pharma executive: "It's one thing not to start a trial. It's another to discontinue an ongoing pivotal trial, which of course is a major decision that involves potentially hundreds of sites, thousands of patients, and millions of dollars. So we have almost a generation of products at risk. It's conceivable that in 2021 we see only 50% of the number of new products approvals that we have been used to, all due to failed approvals due to disrupted pivotal studies from COVID-19." While the ultimate impact on ongoing trials is difficult to estimate at this time, the cost to the industry could be very significant due to timeline delays and additional investments required.

Expanding the use of digital solutions

To try to ensure ongoing research, some companies have undertaken creative approaches, such as moving to remote patient data collection. While many companies are following the FDA's direction to document disruptions to trial management and data collection, many of the attendees agreed that they think that many of these changes—made in an emergency—will end up becoming permanent. Said one executive: "We've been trying to use more remote data capture tools in the past, and now we are finally seeing uptake." Said another, "I would say that the use of decentralized clinical trials and data sharing networks are two areas that I think are going to emerge from this as important aspects of the future."

Talent's shifting priorities

Another emerging trend relates to the movement of talent between larger and smaller companies. Many R&D executives who once saw a lot of upside working at a smaller, pre-IPO startup company have become much more hesitant to move in this uncertain economic environment. "The smaller companies do feel riskier now, I mean, much riskier than they did 18 months ago," said one executive. "What we're seeing is that candidates coming from larger companies are becoming a bit more risk adverse."

Executives think that keeping talent at cash-starved biotechs may become increasingly difficult. However, the participants all believe that the crisis will go a long way toward restoring the reputation and perceived value of a career in science—which will have longer term benefits.

Going forward

The conversation closed on a point of consensus, recognizing the need to establish and share best practices for key research and clinical development activities across the industry. One biotech executive stated that "One thing COVID-19 has done is it's turned us all into a single pharma family. I'm rooting for every other company to succeed. And I think therefore there is more willingness to share best practices."

There is a clear need for biopharma companies large and small to be working far more actively with collaborators including academia, clinical trial sites and CROs to quantify and ameliorate COVID-19 related disruptions as they occur. While hoping that regulatory agencies will stand by their statements to be more forgiving of data integrity problems in future reviews, preventing those issues now should be a high priority. The group identified several existing joint working groups of senior R&D executives as the means to both develop best practices for clinical trial design and management, and to regularly share that work with the FDA and other regulatory agencies. In addition, traditional industry meetings and medical conferences, now potentially meeting virtually, could be forums to share and discuss these new standards. The need for collaboration and leadership has never been greater.

In summary, Zerhouni noted, "There's an old saying that we all use: 'If you think research is expensive, try disease.' And in this case, I would make another slogan: 'if you think preparedness is expensive, try a pandemic.' I would like to see leadership both in what we have accomplished for COVID-19, but also what we need to accomplish in the future. The world cannot go back to the lack of preparedness, lack of coordination, and the chaotic responses that we've had so far."

In a fluid situation where an understanding of the extent of the COVID-19 disruption and how to respond is actively unfolding, this R&D group looks forward to reconvening again in the upcoming weeks to re-appraise the industry's progress.

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Covid-19 Micro-Website

We have launched a micro-website where this and other informative pieces are posted. This site will be regularly updated: click here for further details.

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Our leadership solutions cover individual, team and organizational effectiveness, development and cultural transformation. We work with world-class partners including Sinequanon (SQN), a firm we have invested in that uses AI and advanced analytics to improve workplace culture and performance, and Mobius Executive Leadership, a transformational leadership development firm. In addition, we have partnered with Paradox Strategies, co-founded by Harvard University Professor Linda Hill, to develop the Innovation Quotient (IQ), a proprietary culture diagnostic.

Our goal is that the work we do contributes to successful careers, stronger companies – and a better world.

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