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COVID-19 must catalyse changes to clinical development

The response to the COVID-19 pandemic has shown that exceptional efforts can dramatically accelerate the clinical development of vaccines. We propose that it is time to also take immediate actions to improve clinical trials in other areas to better serve all patients.

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In the few months since the emergence of COVID-19, multiple organizations have engaged with the urgent challenge to rapidly develop a safe and effective vaccine. As one of those organizations, working with our partner BioNTech, we are doing things very differently. And if we succeed, we will develop a COVID-19 vaccine in less than a year, compared with the typical timeframe of 10 or more years for vaccine development[1].

So what, one might say. Extraordinary times deserve extraordinary actions. But how can we take such exceptional action for COVID-19, but not cancer, life-limiting autoimmune conditions or a myriad of other major medical needs? Are these patients somehow less deserving? Of course not.

So what will it take to emerge from the COVID-19 pandemic with a clinical trials ecosystem that better serves patients? Here, we propose actions in two crucial areas: equity in access to clinical trials and awareness of the options available for patients; and speed, efficiency and innovation in clinical development.

Equity in access and awareness

Racial and ethnic disparities in clinical trial populations remain unacceptably abundant, and trust in the health-care system among those who suffer racial injustice is low. It is difficult to find a trial and the requirements for participants are often burdensome, contributing to unacceptably high dropout rates.

It is time to stop the expediency and pragmatism that prevails in patient recruitment and perpetuates inequities, and to find common solutions that build trust and address the socioeconomic barriers to clinical trial participation. We propose commitments to improve access and build trust, and to improve awareness.

Improve access and build trust. We believe that clinical trial populations should reflect the demographics of the countries in which the trials are being conducted, and that no-one should be excluded from a clinical trial by socioeconomic disadvantage alone. Neither of these aims is being achieved today, and things will not change until trust in the system is improved and the systemic barriers to participation are reduced.

We call for a concerted and urgent commitment by sponsors, regulators and policy-makers to reduce the inequities of access to clinical trials that today exclude too many people in need. Actions could include ensuring that people who are under-insured have the opportunity to participate. In addition, to help build trust in racially and ethnically disadvantaged communities, the number of clinical investigators and research site staff from these communities should be increased.

Improve awareness. Patients want to know all potential trials available to them, to make informed decisions and easily connect with study sites. We must create a better solution than we have today. Sponsors should work together with regulators to

provide a simple, plain language, easily searchable and accessible website or app for anyone to find trials that are recruiting and how to take the next steps.

Speed, efficiency and innovation

Sponsors and regulators have been galvanized by the COVID-19 pandemic. Flexibility, boldness in capital deployment, responsiveness, parallel processing and speed in decision-making have been the hallmarks of the work to date. However, the pandemic has also highlighted outdated technical infrastructure, especially the lack of contemporary digital capabilities, slowness of interactions, sequential processes and patchy acceptance of new approaches that have existed for too long at the interface of sponsors and regulators.

We list below four proposals that, if implemented by sponsors and regulators, would benefit all patients.

Sponsors expand adoption of parallel processing at risk. The speed of the COVID-19 vaccine programmes has necessitated massive parallel processing of activities that are usually done sequentially. To give a sense of how radical this is, production capacity of billions of doses must be procured and developed, and commercial procurement contracts and launch plans must be put in place while preclinical and early clinical testing is still in progress and pivotal clinical study designs are being finalized with regulators. Operational decision-making is daily, sometimes hourly.

All of this is only possible through bold deployment of capital with no guarantee of success. But this is what is needed if the goal is to 'do the impossible' and match the speed and quality of drug development to the needs of society. This will redefine the expectations that patients with life-threatening conditions and few if any options will place on sponsors.

Sharing knowledge among sponsors. This has been a welcome feature of the COVID-19 response, but remains limited in scope and poorly coordinated in other areas. Sponsors generally view much of their clinical development activities as competitive information to be carefully stewarded. Yet, if such information was shared, drug development could be accelerated by enabling

sponsors to build on prior and emerging knowledge from others. Competition between sponsors would still exist, but it would be properly focused on the relative benefit/risk to patients of the therapeutic molecules and vaccines themselves.

It is time for sponsors to commit to a new interpretation of what is competitive information and share more. We anticipate that established consortia such as TransCelerate BioPharma will be important in implementing such commitments.

Speed up interactions between sponsors and regulators and fully embrace digital tools. The overnight review of COVID-19 protocols, the waiver of the 30-day investigational new drug (IND) application waiting period and analogous clinical trial application (CTA) provisions, the delivery of scientific advice almost in real time and virtual meetings between sponsors and regulators have all enabled rapid decision-making in response to COVID-19. Unfortunately, this is not true for other diseases where interactions between sponsors and regulators are measured in weeks and months. Regulatory review times are often up to a year.

The timelines being achieved for COVID-19 should be retained for other life-threatening diseases for which available treatment options are few or none. We recognize this will require additional health authority funding to achieve. It should be provided.

Fully embracing digital technology is crucial to enhance access, speed, quality and the patient experience. Examples include wearables and electronic diaries for real-time data capture, image collection by smartphone, telemedicine engagements, remote quality and safety monitoring informed by advanced analytics, and electronic health records as the single source of data to reduce onsite data review and verification.

Regulatory inspections of sites and sponsors can be conducted using secure video and data sharing technologies that allow inspectors to interview personnel, review standard operation procedures and validate source documents and data while assuring compliance with privacy laws.

A single shared cloud-based system for data submitted to regulators could accelerate drug development, enhance transparency and speed-up decision-making[2].

Routine communication can take place by secure email. Dedicated portals, digital vaults and video/audio calls can replace hard-copy mail. For submissions and labelling, regulators can stop requiring original hard copies of documents with wet signatures, notarizations or apostilles that no longer serve a purpose but slow development and can introduce the risk of some prescribers relying on outdated information.

A broad and urgent commitment to digital tools is overdue by sponsors and regulators. We need to let go of familiar but outmoded ways of working, and broadly implement common digital solutions.

Increase collaboration, flexibility, mutual recognition and reliance among regulators. Formal collaboration between regulators should be expanded. For example, simultaneous collaborative review by multiple regulators would not only bring breakthroughs to patients more quickly, but would also help regulators in decision-making by learning from each other.

Greater flexibility is also long overdue. There are many examples, but we list three here. First, sponsors should be able to ship investigational materials before protocol review. Second, rolling IND/CTA submissions should be allowed to facilitate earlier medical reviewer familiarity with the R&D strategy and data. Third, changes in quality systems before regulatory approval should be introduced to allow faster responses to supply challenges and reduce the number of drug shortages. More generally, the existing blanket application of regulatory requirements should be replaced with a fit-for-purpose approach that better serves patients.

Acts of will

Progress is being made in many of the areas we discuss above, but progress without substantive real-world impact is not sufficient. COVID-19 will ultimately deliver many lessons, but the response has already taught us what we are capable of when

the chips are truly down. And yet there are so many patients in dire need from other serious diseases; their conditions are no less deserving, nor their needs less urgent. Put simply, COVID-19 is redefining what our response must be.

We intend to play our full part. We commit that the participants in our clinical trials will reflect the racial demographics of the countries and communities in which we conduct our studies. We commit to expand awareness and access to our clinical trials and to improve the experience of our participants. We commit to share our knowledge more broadly. We commit to fully embrace digital tools for speed and quality.

We encourage other sponsors and global regulators to share their own thoughts and commitments. We should seize this moment, before our conventions re-solidify to the old ways of doing things, to embed the improvements made during the COVID-19 pandemic and accelerate others, on behalf of all patients. If not now, when?

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