How is the pharmaceutical industry responding to COVID-19?

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As pharmaceutical companies work to develop potential vaccines and treatments for COVID-19, they are operating under extreme pressure—as well as the restrictions on movement and interaction that

are affecting all of us. We asked Dr. Greg Licholai, a lecturer at Yale SOM and chief medical information officer at PRA Health Sciences, about the progress toward bringing new drugs to patients.

Is the drug development industry prepared to meet the challenge of a global pandemic?

We are witnessing an impressive response by the global biopharmaceutical industry. As of the end of March there are about 395 clinical research trials for COVID-19 that have been registered in multiple countries, including nearly 120 on the U.S. FDA's ClinicalTrial.gov. Perhaps not surprising that China is conducting at least 180 trials.

There are multiple interventions the industry is exploring. For example, there are 25 vaccine trials, with the first one already enrolling patients in the U.S. An effective vaccine would be used to provide immunity to healthy people in order to prevent infection. Many trials are exploring direct treatments for infected or exposed people. There are 130 antiviral studies using approaches such as nucleotide analogs that prevent viral genetic replication. Additionally, there are anti-inflammation agents as well as antibodies and cell therapies in testing. An old immunosuppressive and anti-parasite drug called hydroxychloroquine is now listed in 19 studies alone or in combinations as a prophylactic against infection.

We should note that the U.S. pharmaceutical industry is large, and its impact reaches well beyond the critical functions of testing, manufacturing. and distributing medications. Directly or indirectly, the industry supports more than 4.7 million jobs with about 300,000 people employed by pharmaceutical and medicine manufacturing companies, according to government statistics. The immediate effect of the crisis

has been a major disruption to work practices. Travel bans and shelter-in-place orders are widely in effect and many corporations have shifted to work-from-home policies. Some big companies such as BMS and Eli Lilly have announced suspension or delay of some of their clinical development programs in order to keep their people safe.

How long will it take to develop new vaccines or treatments, and what steps can accelerate the process?

Usually it takes years to bring new drugs to patients. However, regulatory agencies are permitting accelerated measures to help speed the development of medications. The U.S. FDA, European EMCDDA, and Chinese CDE are all using special emergency clinical trial approval processes for COVID-19 and a number of products have already quickly moved through the systems. Apparently, the fastest approval took only 19 hours from submission by three professional groups that simultaneously initiated review.

Vaccines can take over a year to develop under the best of circumstances. The first vaccine to begin human testing was Moderna's mRNA-based drug, which went into volunteers on March 16 after only weeks in preclinical development. Although the vaccine is likely over a year from widespread rollout, the company believes it may be made available to healthcare workers as early as this fall. Other companies believe they will begin human testing within a month, and more vaccines will go into the clinic by November.

Several sponsors are taking advantage of antiviral drugs that could be useful in treating COVID-19. One of the more public episodes concerns a drug called remdesivir that had antiviral activity against RNA viruses such as respiratory syncytial virus (RSV) as well as others like Ebola. The manufacturer, Gilead, initiated an emergency access program to

treat a small number of patients while it ramped up larger clinical trials. However, they were forced to withdraw the access program when overwhelmed by demand, indicating the risks of companies inadvertently building up expectations during desperate times.

Just recently the FDA has granted emergency approval of two new PCR-based molecular rapid diagnostic tests for use in temporary screening facilities, doctor's offices, and nursing homes. These could provide results in under an hour. Unfortunately, approval does not mean availability, and now the product manufacturers must scale up to begin distribution. The healthcare giant Roche last week announced shipments of the first 400,000 COVID-19 tests to laboratories across the U.S. to begin patient testing under FDA Emergency Use Authorization.

Is the pharmaceutical industry making use of digital tools during this crisis?

There has been a swift response by the biopharmaceutical industry to begin embracing new digital and remote monitoring techniques. Travel restrictions, quarantines, and avoiding public places makes it extremely difficult to perform many professional and medical activities and is particularly challenging for healthcare visits and conducting or participating in clinical research. We are seeing an acceleration in the rolling out and scaling up of internal R&D digital transformation efforts such as remote monitoring using platforms such as virtual clinical trials.

Remote patient monitoring (RPM) is a useful strategy to provide effective clinical care while maintaining safety and public health controls during difficult times. RPM includes the use of telemedicine, connected devices, mobile platforms, and smartphones to ensure that patients and care providers are able to remain connected at a distance. Many provider organizations are quickly investing in RPM solutions to

track and manage infected, unstable, or high-risk patients.

The FDA recently issued guidance on conduct of clinical trials during the pandemic to ensure the safety of trial participants and professionals while maintaining data integrity. They urged sponsors to use alternative methods for safety assessments, which include phone contact, virtual visits, and use of local labs or imaging centers. The agency also issued a new policy that allows manufacturers of approved non-invasive, vital sign-measuring devices to expand their use so that healthcare providers can use them to monitor patients remotely. The devices include those that measure body temperature, respiratory rate, heart rate, and blood pressure.

The Association of Clinical Research Organizations (ACRO) has issued recommendations to sponsors, CROs, and hospital sites to introduce emergency interim measures so that clinical trial monitoring is maintained during the crisis. In addition to moving toward telephone and telemedicine contacts, they recommend implementing such digital tools as electronic patient recorded outcomes (ePROs) and e-diaries.

Totally decentralized or virtual clinical trials take a while to design, plan, and implement. The first fully virtual drug approval trial, called CHIEF, was kicked off by Johnson & Johnson (JNJ) for the treatment of heart failure just a few of weeks ago. (I helped JNJ design the study.) Since the CHIEF launch, virtual trials have attracted the attention of many sponsors who now are rushing to see how they can accelerate similar techniques for their entire portfolio of programs.

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