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DEVELOPING A CORONAVIRUS VACCINE – THE MOST URGENT SHARED ENDEAVOR OF OUR LIFETIMES: PART 2

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WHERE ARE UP TO NOW WITH DEVELOPING AND TESTING A COVID-19 VACCINE AND WHAT HAVE WE LEARNED SO FAR?

Vaccine development is moving extremely quickly and almost every day we hear news on this topic. By the end of April more than 90 vaccine candidates had been disclosed. Below we summarize some information about vaccines which had entered clinical testing by late May 2020.

CanSino Bio are furthest ahead in the race to develop a COVID-19 vaccine, collaborating with the Academy of Military Sciences in China. Their vaccine Ad5-nCoV is an adenovirus type-5 vector-based recombinant COVID-19 vaccine which entered its first-in-human trial in mid-March in healthy volunteers in the city of Wuhan, then the epicenter of the outbreak. On April 9, 2020, the company announced that they were ready to advance into Phase II testing – this has now begun in China. CanSino are the first to publish their Phase I data in 108 participants which show that Ad5-nCoV is tolerable and immunogenic at 28 days post-vaccination.

Sinovac Biotech based in Beijing, China are testing a vaccine based on inactivated virus and on April 17 the company announced that their Phase I trial in 144 healthy volunteers had begun recruiting in Jiangsu Province. Sinovac Biotech were the first company in the world to market a vaccine for the H1N1 swine flu and so have very relevant experience. Initial studies in non-human primates have shown the vaccine to be safe and 100% protective in a limited number of animals.

Moderna Inc., a biotechnology company based in Cambridge MA, have collaborated with investigators from the Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health (NIH) to develop an mRNA vaccine, mRNA-1273, which encodes for a prefusion-stabilized form of the spike protein present on COVID-19. Moderna scientists had already been working on a vaccine targeting the spike protein in the MERS (Middle Eastern Respiratory Syndrome) coronavirus and this gave them a great head start. The company opened a Phase I trial (NCT04283461) in healthy volunteers in Seattle in mid-March and on 18 May 2020 they reported positive interim Phase I data and noted a Phase III trial is expected to start in July.

Inovio Pharmaceuticals, a biotechnology company based in Plymouth, PA, also has experience with coronaviruses which has given them a head start in developing a DNA vaccine, INO-4800. On April 28, Inovio reported that their Phase I trial being conducted in Philadelphia and Kansas City was fully recruited, with interim immune responses and safety results expected in late June. Preclinical data have been recently published which show robust neutralizing antibody and T-cell immune responses to the vaccine. Inovio are hoping to initiate a Phase II/III trial in July/August.

Researchers at the **University of Oxford**, UK have used their experience in vaccine development to construct ChAdOx1 nCoV-19 which is an adenovirus vector vaccine including genetic material from the COVID-19 spike protein. The researchers have already given vaccines made from the ChAdOx1 viral vector to several hundred people and it has been safe and well tolerated. An ongoing Phase I trial will recruit up to 1102 participants in Oxford, Southampton, London and Bristol, UK with the first doses given on 23 April. On 30 April, an agreement with **AstraZeneca** was announced, under which they assumed responsibility for development, worldwide manufacturing and distribution of the vaccine. As with Sinovac, non-human primate studies have shown the vaccine to be safe and 100% protective. The University of Oxford team are now looking for 10,260 people to participate in the Phase II/III trial. AstraZeneca have announced that they have secured total manufacturing capacity for one billion doses of vaccine so far and will begin first deliveries in September 2021.

On 29 April, **Pfizer** and **BioNTech** announced that they had dosed participants in the first cohort of a Phase I/II clinical trial of COVID-19 mRNA vaccine candidate BNT162 in Germany and on 5 May the first US subjects were reported to have received the vaccine. BioNTech and Pfizer are jointly developing BNT162. During the clinical development stage, BioNTech will provide its partner's clinical supply of the vaccine from its GMP-certified mRNA manufacturing facilities in Europe. BioNTech is collaborating with Fosun Pharma to develop BNT162 in China, where the companies expect to conduct trials.

Shenzhen Genoimmune Medical Institute has begun clinical trials of two vaccines based on lentiviral vectors with immune cells that are genetically modified to target the COVID-19 spike protein. Two Phase I trials (NCT04276896 and NCT04299724) are in progress in Shenzhen, Guangdong, China.

On 25 May, 2020, yet another company entered the clinical testing phase. **Novavax** announced enrolment of the first participants in a Phase I/II clinical trial of NVX-CoV2373 – this vaccine uses recombinant nanoparticle technology to generate antigen derived from the coronavirus spike protein and also contains Novavax' proprietary Matrix-M™ adjuvant to enhance immune responses. The company expect to see preliminary immunogenicity and safety results from the Phase I portion of the trial in July 2020.

IS THERE ENOUGH MANUFACTURING CAPACITY AVAILABLE TO PROVIDE THESE VACCINES TO THE WORLDWIDE POPULATION ONCE THEY HAVE BEEN APPROVED?

Millions of doses of COVD-19 vaccine will be needed – potentially 300 million in the US alone – so it is essential to plan ahead to ensure that any successful vaccine can be rolled out across the world. The supply chain will include not only the vaccine itself but also the raw materials needed to make vials, syringes and needles. Consideration also needs to be given to transport and storage – for instance RNA or DNA vaccines might have different storage and refrigeration requirements because the technology has never been used for an approved vaccine before. Medical suppliers will need to increase their capacity and, as raw materials and components come from many different parts of the world, seamless exporting and shipping of materials across borders will be essential.

Smaller companies developing COVID-19 vaccines do have the infrastructure to manufacture and distribute them worldwide and this has driven a number of collaborations with larger Pharma companies or other organizations who can bring the resources and funding needed. For instance in April, BARDA awarded up to $483 million to Moderna to fund the advancement of mRNA-1273 up to FDA licensure. Moderna have also found another partner in **Lonza** who have agreed that their facilities in the US and Switzerland can be used for manufacturing, possibly as early as July and AstraZeneca have assumed responsibility for developing and manufacturing the ChAdOx1 nCoV-19 created by researchers at the University of Oxford.

Sanofi and **GSK**, leading vaccine companies, have announced a collaboration to develop an adjuvanted vaccine for COVID-19, using innovative technology from both companies. The companies plan to initiate phase I clinical trials in the second half of 2020 and have also set up a Joint Collaboration Task Force which will seek to mobilize resources from both companies and accelerate vaccine development.

Johnson & Johnson is collaborating with BARDA on rapid scaling of the Company's manufacturing capacity with the goal of providing global supply of more than one billion doses of a vaccine. Human studies on J&J's lead vaccine candidate are anticipated by September 2020 at the latest the first batches of a COVID-19 vaccine could be available for emergency use authorization in early 2021.

J&J has also signed agreements with two manufacturing companies – **Catalent** – who will accelerate availability of manufacturing capacity at their facility in Bloomington, Indiana and **Emergent BioSolutions, Inc**. to provide drug substance manufacturing services in 2020 and potentially support commercial manufacturing in the future.