Insight

COVID-19 VACCINES, THERAPIES AND TESTING: A ROADMAP TO NORMALITY

Leaves outside our office windows in St. James's are starting to turn colourful. Fall is coming, and so is the second wave of the SARS-CoV-2 virus which has resurged in recent weeks in many countries. Once again, our focus has turned to vaccines for solutions to liberate us from being hostages to COVID-19.

Back in July, we wrote an insight entitled *The Race for a COVID-19 Vaccine*. Significant progress has been made by scientists since then.

In this document, we provide our latest insights on the status of vaccine development, the likely timing of vaccines available to us, and how vaccines will be rolled out. We also discuss the advances in therapeutic treatment of COVID, and look at promising therapies that can be used to reduce the severity of the disease and thus act as a critical bridge before vaccines arrive. Finally, we provide our perspective on a roadmap for ending the pandemic and returning our lives to normality.

Vaccines: The Current Status of Vaccine Development

According to the World Health Organisation (WHO), as of September 30, there are 192 vaccine candidates in development, more than 40 in clinical evaluation and 10 in phase three (the last stage of clinical development before approval). In our July insight, we introduced different vaccine technology platforms and the characteristics of each. Amongst the 10 most advanced clinical programmes, four are non-replicating viral vector vaccines, three are inactivated vaccines and two are mRNA vaccines. By developing vaccine candidates using different technology platforms, the world will have more shots on goal to obtain one or more efficacious and safe vaccines.

Table 1 The Most Advanced Vaccine Programs Worldwide

Technology Platform	Live Attenuated Vaccines (LAV)	Inactivated Vaccines (IV)	Recombinant Protein Vaccines (RPV)	Replicating Vector/ Non-replicating Vector Vaccines (RVV/NVV)	Nucleic Acid Vaccines (DNA/mRNA)
Companies in phase III trials		Wuhan Institute of Biological Products sinovac Beijing Institute of Biological Products	NOVAVAX	AstraZeneca / OXFORD CanSinoBIO Gamaleya Research Institute of Epidemiology and Microbiology Johnson&Johnson	moderna / NIH Pfizer / BIONTECH / FOSUNPHARMA
Selective companies closely behind			Anhui Zhifei Longcom SANOFI / gsk		CUREVAC

J. Stern & Co
4 Carlton Gardens
London SW1Y 5AA
United Kingdom

Tel: +44 20 3478 1800
Fax: +44 20 3478 1799
info@jsternco.com
www.jsternco.com

Most Advanced Vaccine Programmes

In the US and Europe, the three most advanced programmes are from Pfizer/BioNTech, Moderna/NIH and AstraZeneca/Oxford University and all are well into their respective phase III trials. In earlier phase1/2 clinical testing, all three vaccine candidates generated neutralising antibodies and antibody titre at levels equal to or greater than those produced by patients who have recovered from COVID-19. All three vaccine candidates generated a T-cell response which is important for our body to fight the infection. These vaccine candidates were well tolerated, whilst side effects were largely mild and moderate, and were transient.

Table 2 The Most Advanced Vaccine Programs in the West

Vaccine Candidates	Pfizer / BIONTECH	moderna / NIH	AstraZeneca / University of Oxford
Start time for phase II/ III trial	July/2020 (US)	July/2020 (US)	August/2020 (US) May/June 2020 (ex-US)
Dosing	Two Doses, prime and booster 21 days apart	Two Doses, prime and booster 28 days apart	Two Doses, prime and booster 28 days apart
Planned number of people enrolment in the trial	30,000 original plan, expanded to 44,000 in September	30,000	30,000 in the US 12,330 in the UK 5,000-6,000 in Brazil 2,000-4,000 in South Africa
Estimated enrolment diversity (%)	24-48%	25-40%	Not disclosed
Interim and final analysis	Four interim analyses at 32, 62, 92 and 120 events Final analysis at 164 events	Two interim analyses at 53 and 106 events Final analysis at 151 events	One interim analysis at 75 events Final analysis at 150 events
Estimated earliest time for Emergency Use Authorisation (EUA) filing	October/2020	November/2020	Not disclosed, estimated November-December/2020
Estimated earliest timing for EUA approval	Q4/2020	Q4/2020-Q1/2021	Q4/2020-Q1/2021
Doses available in 2020	100m doses	Not disclosed	700-800m doses (including 400m doses delivered by Serum Institute of India to low income countries)
Doses available in 2021 and beyond	1.3bn doses per annum	Up to 1bn doses per annum	2bn doses (including 1bn doses delivered by Serum Institute of India for low income countries)
Vaccine storage	Stable at -70°C 15 days in refillable dry ice shipper 5 days at 2-8°C 6 hours at room temperature	Stable at -20 °C 7 days at 2-8 °C 12 hours at room temperature	Stable at 2-8°C

Regulatory Requirements for Vaccine Approval

Phase III clinical trials are much larger in size and include a greater proportion of older people (age >65) and people with increased risk of complication from COVID-19, as well as more diversity in ethnicity and race. Trials are randomised, double-blind and placebo controlled. The test of efficacy is based on statistical analysis of the number of symptomatic infections that have occurred in the vaccinated arm compared to that in the placebo arms. Infections are confirmed by the positive PCR virus (antigen) test and by at least one or two symptoms of COVID-19. The timing of the trial completion is event driven and based on the number of symptomatic infections. The safety of these trials is monitored continuously by the independent Data and Safety Monitoring Board (DSMB).

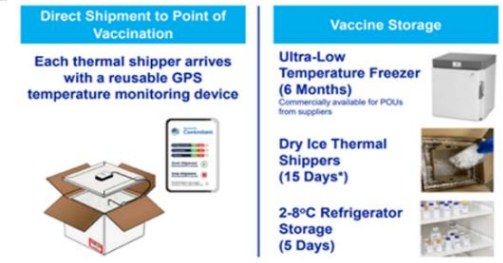
The trial design has a number of interim analyses to assess the efficacy. At each interim analysis, DSMB will take a look at the trial efficacy data and will either allow the trial to continue or to stop. The latter happens either on the grounds of safety concerns or of efficacy results — for example, if a trial shows overwhelming efficacy, making it unethical to continue with the trial for people on the placebo arm, or if a trial has little chance of meeting the required efficacy end point.

There are some differences in trial designs amongst the three leading companies but they are all aimed at achieving the efficacy target of 50% (with lower bound of confidence interval greater than 30%) set by the FDA. The most updated guidelines by the FDA also require at least 2 months of median safety follow-up after completing the vaccination, combined with at least 5 severe COVID infections in the placebo arm as well as a certain number of infections in elderly people, before the regulatory review for an Emergency Use Authorisation(EUA) can take place. For full approval, the FDA requires at least 6 months safety follow-up.

If a vaccine, for example, has an efficacy of 60-70% (i.e. above 50% required by the FDA), it is estimated that around 100 events are needed to produce data required for filing of an EUA. If, however, a vaccine has a much higher efficacy, less time is needed to achieve the statistically significant efficacy end point. This will warrant an earlier filing with the regulators.

When will the Most Advanced Clinical Trials Report Efficacy Data?

Pfizer/BioNTech (mRNA vaccine) — The company started phase III trials on July 27 in the US. The trial design has the potential to generate earlier efficacy data given that the two-dose regime is 21 days apart, it has a more immediate observation period for efficacy (7 days after the second dose) and a more frequent interim analysis (4 interim analyses). Thus, the design gives more and earlier opportunities to take a look at the efficacy data. Recently, Pfizer expanded its trial of 30,000 enrolments to 44,000, partly to include younger cohorts (under the age of 18) and partly to speed up the event rate. It is likely that the first interim analysis (i.e. after 32 infections have occurred) will take place in mid-October. In an open letter, Pfizer CEO Albert Bourla announced that the company will have the vaccine data ready for EUA filing in October. This suggests Pfizer/BioNTech's vaccine is more efficacious than 60-70%. In addition, Pfizer/BioNTech has initiated rolling submission to



Source: Pfizer

the European Medicines Agency for its SARS-CoV-2 vaccine where clinical data will be reviewed as it becomes available, before a complete application is submitted. This will speed up the review time from the normal regulatory process.

Whilst Pfizer/BioNTech's mRNA vaccine is likely to be the first granted with an EUA, it requires cold storage and presents some logistical challenges. Pfizer has developed a distribution plan which includes direct shipment of dry-ice thermal shippers with reusable GPS temperature monitoring devices to the point of use (POU).

Moderna/NIH (mRNA Vaccine) — The phase III trial also started on July 27 in the US. The trial design includes two doses 28 days apart and a longer period of wait time (14 days after the second injection) to observe efficacy. The trial design has two interim analyses. The first interim analysis (i.e. after 53 infections have occurred) will be later than that of Pfizer/BioNTech. At the Investor Day in September, the company announced it is slowing down its phase III trial enrolment to increase the diversity pool.

It is likely that the first interim analysis will take place in early November. CEO Stéphane Bancel told the *Financial Times* in late September that the company will not be able to file for an EUA until 25 November at the earliest. Rolling submission is also planned for Europe.

AstraZeneca/Oxford (Viral Vector Vaccine) – The company has ongoing trials both in the US and elsewhere. The ex-US trials (UK, Brazil and South Africa) started in May/June, two months earlier than its US trial. The UK trial targets an enrolment of 12,330 volunteers, whilst the numbers for Brazil are 5,000-6,000, and 2,000-4,000 for South Africa.

AstraZeneca/Oxford's trial design is a two-dose regime 28 days apart, but only has one interim analysis for efficacy after 75 infections have occurred. Therefore, it does not allow an earlier look at the efficacy data. Despite an earlier start, we understand the event rate has been slow to accumulate in the UK. Recently, the *Financial Times* reported that the UK is to start a human challenge trial in London led by investigators at Imperial College, with a different vaccine candidate, where volunteers are deliberately infected by the virus to speed up the development programme.

AstraZeneca/Oxford's vaccine candidate had two adverse safety cases which prompted various DSMBs to pause the clinical trials worldwide. The first case was not vaccine related, but the second relates to a rare neurological side effect potentially caused by the vaccination. After a brief investigation, trials in the UK, Brazil and South Africa have been given permission to resume but the US trial remains on hold at the time of writing. We understand that the FDA has requested further clinical data on other vaccine candidates developed by the University of Oxford using the same viral vector in the COVID-19 vaccine, presumably to better understand if the adverse safety event is caused by the technology platform, in this case the viral vector (carrier of the vaccine) or by the vaccine itself.

Given the pause of the trials, the second dose for some volunteers may have been missed. It is likely additional enrolment will be needed to complete the trial. This creates additional uncertainty for the timing of the efficacy data. Our best estimate is November at the earliest, for ex-US trials, assuming AstraZeneca can pool its international trial data from different countries. If safety was not an issue, we anticipate the earliest time for an EUA is late 2020 or early 2021.

Other Advanced Vaccines in Development

It is worth mentioning a number of other COVID-19 vaccines under development that have manufacturing scale and are closely behind.

Johnson and Johnson (Viral Vector Vaccine) — Phase III started in September with a single dose regime. The company plans to enrol 60,000 volunteers both in the US and further afield, with different ages and ethnicities. The one-dose regime offers a great deal of simplicity and convenience for mass vaccination, and the same viral vector technology is used in the company's Ebola vaccine. This has recently been approved for use in Europe and has already been given to over 100,000 people without severe side effects. The vaccine is stable for 2 years at -20ºC, and for at least 3 months at 2-8ºC. On October 12, the company announced that it has paused its phase III trial due to one adverse event. The DSMB is currently investigating if the case is vaccine related. Assuming the case does not cause serious safety concerns, the goal is to file for an EUA in early 2021. The company has capacity to supply 1 billion doses per year, starting in 2021.

Sanofi/GSK (Protein Vaccine plus an Adjuvant) — Phase I/II started in September with a two-dose regime involving 440 volunteers. The company plans to move to a phase III trial in December 2020 and to seek regulatory reviews in H1 2021. This is a proven technology platform where multiple vaccines have been marketed using the same technology and adjuvant. We understand the vaccine is stable under refrigerated conditions, and the company has capacity to produce 1 billion doses per annum.

Novavax (Protein Vaccine plus an Adjuvant) – Phase III trial started in September in the UK with a target recruitment of 10,000 volunteers, 25% of whom will be aged above 65. The trial will be a two-dose regime. The vaccine is stable at 2-8ºC, and manufacturing will be carried out in seven different countries, with an aim to produce 100m doses in Q1/2021 and 1-2 billion doses in 2021.

Others - The vaccine developed by Gamaleya Research Institute, Sputnik V, has already been approved for use in Russia, while the Chinese authorities have approved the vaccine developed by CansSino Biologics for military use, and CoronaVac by Sinovac for emergency use in high risk populations.

Vaccines: Potential Timing of Authorization

The FDA has scheduled an advisory committee meeting on October 22 to discuss COVID-19 vaccines. Although data from specific vaccine candidates is unlikely to be available for the meeting, with the exception of a small chance from Pfizer/BioNTech, we expect broader discussions on the framework of approval and Emergency Use Authorization (EUA), and the trade-off between the risk and benefits, and the long-term follow-up of safety and vaccine durability.

Assuming vaccines are shown to be effective and safe, we expect an EUA will be granted in late 2020 and early 2021 to the three most advanced vaccine candidates, and vaccination can begin.

Full approval will require a longer-term follow-up (minimum 6 months) on safety post the EUAs.

Vaccines: Potential Roll-Out and Availability

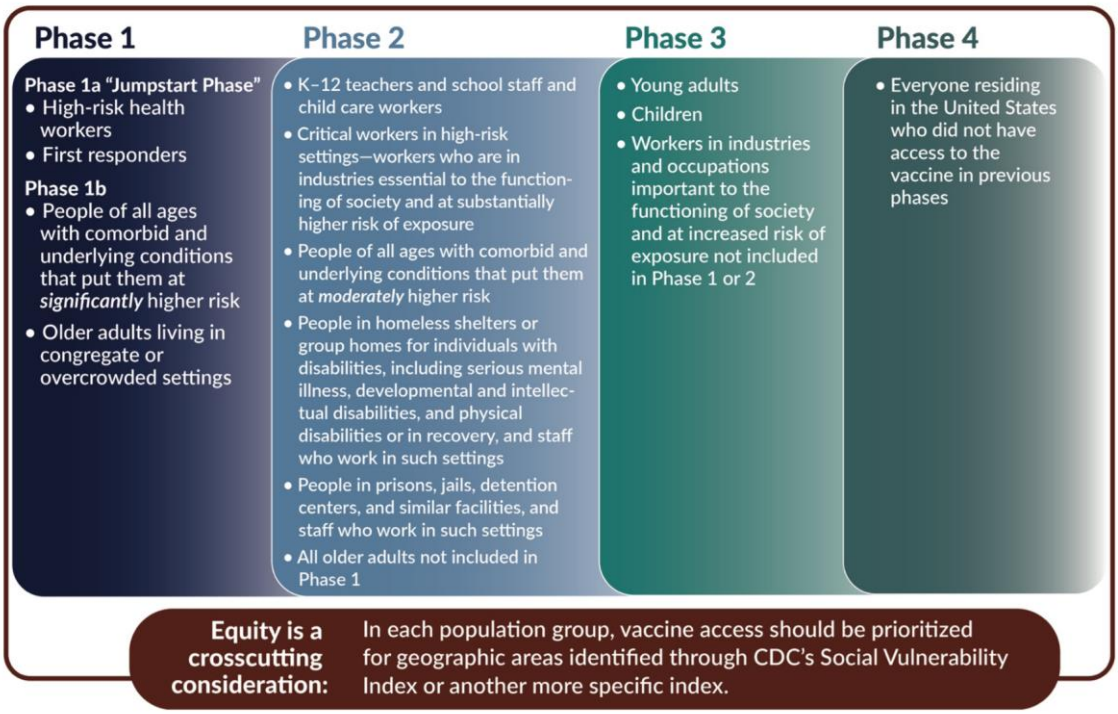
At the time of the launch of the first wave of vaccines, we expect supply will be limited. It is important to allocate vaccines ethically and priority should be given to those most at risk.

Phased Approach with Priority Given to Most at Risk

The WHO, in collaboration with the Strategic Advisory Group of Experts (SAGE) on Immunisation, has developed a value-based framework which recommends a phased approach to vaccine distribution.

In the US, the National Academies of Science, Engineering and Medicine published an ethical framework based on lessons learnt from the previous mass vaccination campaigns, and the allocation of scarce medical resources during the COVID-19 pandemic. The framework recommends a phased approach, with best efforts made to complete each phase before moving to the next. The general principle is to give priority to those who are most at risk of developing a severe illness, and to workers on the front line.

The Advisory Committee on Immunisation Practices (ACIP) from the Centres for Disease Control and Prevention (CDC) held a public hearing on August 26 about the plan for vaccine rollout, and a vote on this interim prioritisation vaccination scheme is expected soon.



Source: The National Academies of Science, Engineering and Medicine, The National Academies Press 2020

Elsewhere, we expect other governments will follow a similar prioritisation and phased approach. In the UK, the Joint Committee on Vaccination and Immunisation (JCVI) published an interim report in September. The committee strongly agree that a simple age-based programme will likely result in faster delivery and better uptake of vaccines in those at the highest risk. The interim ranking of priorities, which is a combination of clinical risk

stratification and an age-based approach, should optimise both targeting and deliverability. A provisional ranking of prioritisation (11 in total) puts older adult residents in a care home and care home workers first, followed by people aged 80 and above, as well as healthcare and social care workers.

Treatment: The Current Status of Development of COVID-19 Treatment

Whilst vaccine development is full steam ahead and the first vaccine is close to being in sight, scientists are also working around the clock to find appropriate COVID-19 treatments on a separate track. Effective therapies can provide a bridge to prevent patients becoming severely ill, reducing hospitalisations and the mortality rate before a vaccine becomes available. In this section, we discuss the advances in therapies for COVID-19 treatment.

COVID-19 Disease Manifestation

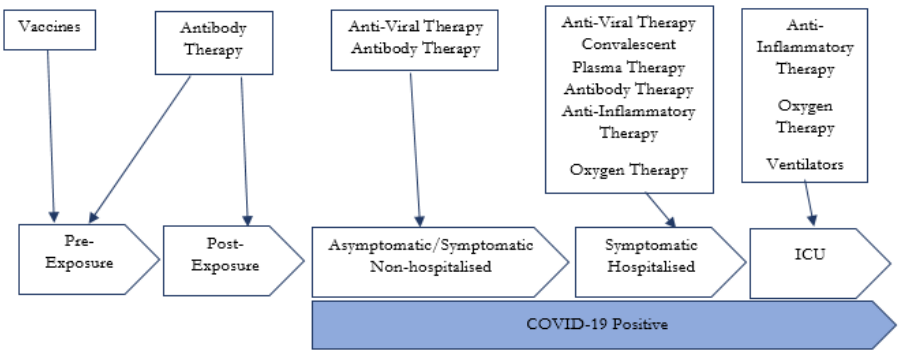
To develop a treatment therapy for COVID-19, we need to first understand how SARS-CoV-2 virus makes us ill. It happens in two phases, the **infection phase** and the **inflammation phase**.

Infection Phase — During the infection phase, the virus enters our body through the upper respiratory tract (nose, mouth), attacks our cells and rapidly replicates. If our body is unable to mount a successful defence at this stage, the virus travels down to the lower respiratory tract (lungs) causing more severe diseases like pneumonia.

Inflammation Phase — Fatality often occurs during the inflammation phase of COVID-19. The normal anti-viral immune response requires the activation of the inflammatory pathways of our immune system. However, excessive production of pro-inflammatory cytokines can lead to acute respiratory distress syndrome (ARDS), a condition where the lungs become severely inflamed and fluid from nearby blood vessels leaks into tiny air sacs in the lungs, making breathing increasingly difficult. Mortality in COVID-19 patients has been linked to the presence of the so-called "cytokine storm" which could cause tissue damage and organ failure.

Treatment Options

Treatment solutions targeting both the infection phase and inflammation phase of the disease manifestation have been sought. We summarise below some key treatment options developed by scientists, and a schematic diagram of disease management.



Antibody Therapy — The body's fight of a COVID infection starts with the race between the virus and our immune response. Most of the time, our immune system wins the race but not always, and often not quickly enough. Antibodies are the first defence our body launches in this race. They work by binding to the virus and stopping it from entering the cell (i.e. they neutralise it). But it could take several days for our body to generate them whilst the virus replicates rapidly. Antibody therapy is designed as the substitute to our natural immune response, and if given, can launch an immediate attack on the virus before we are able to, helping our body to win this race.

The past success using antibodies to treat Ebola and MERS patients validated this approach. It could provide a treatment bridge before a vaccine becomes available, and work for those who could not tolerate or do not respond to the vaccination even after a vaccine is on the market.

However, antibody therapy is much more expensive than a vaccine and its effect may be shorter in duration. It typically lasts for a few months, but can be re-administered to boost the immunity.

Antibodies can come from donated convalescent plasma of patients who have recovered from COVID-19 (plasma therapy) or from mass-produced potent mono-antibodies, or an antibody cocktail selected from convalescent plasma by scientists.

Several companies are developing antibody therapy. Regeneron/Roche, Vir/GSK and Eli Lilly/AbCellera/Junshi have already advanced their programs. AstraZeneca is closely behind and Celltrion also entered the clinical phase in the summer. While we expect multiple antibody therapies will eventually be on the market, Regeneron/Roche and Eli Lilly/AbCellera/Junshi are the most advanced.

Regeneron/Roche — Regeneron has reported encouraging interim phase III results in one of the three ongoing trials. The data showed that the antibody cocktail reduces the viral load and the time to alleviate symptoms in non-hospitalised patients with COVID-19. The study also showed a positive trend in reducing medical visits. The antibody cocktail had the greatest benefit in patients who tested low/no antibody in the blood (sero-negative) before starting the therapy. The latter is particularly encouraging as sero-negative patients are more vulnerable to the disease worsening, so it was good to see the antibody therapy working where it is most needed. Regeneron/Roche is also exploring the antibody use in hospitalised patients, as well as in prophylaxis use in household contacts of infected individuals.

Eli Lilly/AbCellera/Junshi — This group led by Lilly has filed a request for EUA of its mono-antibody therapy for high risk patients with mild and moderate COVID-19. It is also conducting a trial with a two-antibody cocktail. Interim results showed both mono-antibody therapy and the cocktail reduced viral load, symptoms and COVID-related hospitalisations and ER visits. It plans to file for an EUA request for the antibody cocktail in November. On October 13, another trial involving the mono-antibody in combination with Remdesivir in hospitalised patients was paused due to potential safety concerns. The DSMB is currently investigating this case.

AstraZeneca — The company announced it is initiating two phase III trials of its long-acting two antibody cocktail in more than 6,000 participants. The trials will evaluate the safety and efficacy of the antibody cocktail for prevention as well as for treatment of COVID-19. The antibody is engineered with a durability of 6 to 12 months.

Anti-Viral Therapy — Once the virus enters our cells, it rapidly replicates, causing infection. Anti-viral drugs reduce/prevent viral replication and give the body more time to kill the virus. Some experts believe that antiviral drugs have greater efficacy when given earlier in the course of the disease.

Veklury (Remdesivir) — The drug was developed by Gilead and showed an improvement in clinical recovery versus standard care. Although its effectiveness is modest, it has received an EUA from the FDA for treatment of patients with moderate COVID-19.

Avigan (Favipiravir) — from Fujifilm is an antiviral drug used to treat flu in Japan. It was also found to be effective in treating Ebola. It was first used by Chinese doctors in Wuhan to treat COVID-19 patients and has since been approved for emergency use in a number of countries to fight mild and moderate COVID-19.

MRK-4482 — Merck's antiviral drug is in phase II/III in both hospitalised and non-hospitalised patients. Both trials are expected to read out in April 2021.

Anti-Inflammatory Therapy — Once patients have been hospitalised with acute respiratory distress syndrome (ARDS), anti-inflammatory drugs such as *dexamethasone* and *hydrocortisone*, both corticosteroids, are used to dampen patients own immune responses.

Dexamethasone — the drug has been used to decrease inflammation in several different conditions since the 1960s. Results from the RECOVERY trial in the UK demonstrated that dexamethasone reduced the mortality by one third for patients on ventilators, and by one fifth for those on oxygen therapy.

Hydrocortisone — Research headed by Professor Anthony Gordon from Imperial College showed that hydrocortisone led to a 93% chance of a better outcome when treating critically ill patients in intensive care.

Other anti-inflammatory drugs — The IL-6 class of drugs (Acetemra from Roche and Kevzara from Sanofi/Regeneron), unfortunately has failed to show definitive efficacy in recent trials. Further trials of Acetemra, in combination with Remdesivir, are ongoing. JAK-inhibitors are another class of anti-inflammatory drugs currently being studied for COVID-19.

Testing: Do We Still Need Testing Once Vaccines Become Available?

At present, testing is one of the main tools used in the surveillance of the virus, and in diagnosing infections. We believe even after mass vaccination, continued testing will still be needed for surveillance of disease outbreaks, and more importantly the detection of mutations of the virus.

Durability of Vaccination

For a start, we do not know the durability of any vaccine. We know that the antibody level of people who had COVID-19 starts to wane after 2-4 months, but we do not know if their immune system can still launch a response from the memory when attacked by the virus once again. Several cases of re-infection with SARS-CoV-2 have been confirmed, although the re-infection appeared to be by a different strain. In all but one case, re-infection was asymptomatic, suggesting pre-existing immunity is protective against the disease. One incident of re-infection caused a more severe disease that required hospitalisation. Further

investigation is needed, in particular to answer the question of potential presence of antibody-dependent enhancement (ADE). Under ADE, the virus binds to sub-optimal antibodies which enhances its entry into the cell, potentially causing a more severe disease.

Mutations of the Virus

So far mutations of SARS-CoV-2 are rare, but a few have been identified in Spike Protein which is the target that all vaccines in development are based on. Although these mutations are small in number and do not impact the effectiveness of vaccines currently in development, we anticipate the virus will continue to mutate as we develop immunity to it.

Non-Responders to Vaccine

Vaccines are unlikely to have 100% efficacy. Some people may not respond to vaccination. A typical flu vaccine has an efficacy of around 40-60%. The efficacy bar set by the FDA for COVID-19 is 50%, with the lower bound at only 30%. Antibody tests can be used as companion diagnostics to determine if a vaccination generates adequate antibody responses.

Non-Vaccinated Population

People with underlying conditions who could not tolerate or are unwilling to take vaccinations still present a risk of infection and disease manifestation, although the former may be given antibody therapy instead.

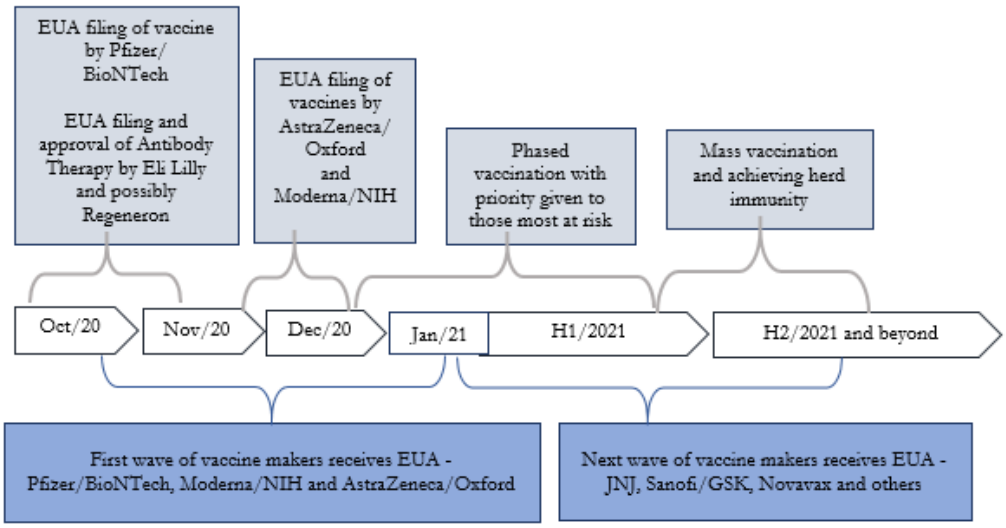
Our Perspective: A Roadmap to Normality

With the improvement in therapeutic treatments across the disease spectrum, the availability of vaccines, and increased capacity for testing and surveillance, we are moving closer and closer to getting COVID-19 under control.

We anticipate the first wave of vaccines to be available in late 2020 or early 2021. Most governments will follow the principle of ethical allocation of vaccines and adopt a phased approach, with priority given to those most at risk and essential workers such as healthcare/care workers and those in the emergency services.

We anticipate the second wave of vaccines to be available in the first half of 2021. This will increase the supply of vaccines significantly and allow broader access to vaccinations for the population.

Depending on the availability of vaccines and the speed of rollout, there is a chance that herd immunity could be achieved sometime in the second half of 2021 in the US and Europe. Below is our best estimate of the roadmap to normality.



Our society cannot return to normality if the population is not willing to get vaccinated. We expect public health authorities to launch vaccination campaigns to assure the public of the safety of vaccines. Chief executives of nine drug companies have already signed a pledge promising not to file for regulatory approval or authorisation of their vaccines until they are shown to be safe and effective.

No country will be safe until the entire world has access to the vaccine. COVAX, launched in April by the WHO, the European Commission and France, brings together governments, global health organisations, manufacturers and scientists, the private sector, civil society and those working in philanthropy, with the aim of providing innovative and equitable access to COVID-19 diagnostics, treatments and vaccines.

The Gavi COVAX Advance Market Commitment (AMC) programme ensures that the 92 middle and lower-income countries that cannot fully afford to pay for COVID-19 vaccines themselves get equal access to them as higher-income countries, and at the same time. At the time of writing, 76 upper middle-income and high-income countries have submitted confirmations that they intend to participate. The AMC has raised about US$1.8 billion of the initial seed capital target of US$ 2 billion needed by the end of 2020.

Many experts believe SARS-CoV-2 will be living with us for a long time but treatments and vaccines will make it a less severe disease, comparable like a common cold. It is also possible regular boosters will be required to renew immunity, similar to that of seasonal flu. Scientists are already starting to look at ways of improving treatment and designing better vaccines.

Whatever lies ahead, we are much better equipped today than ever before to deal with COVID-19. The end of this pandemic, and a return to normality, are very much within our reach.

Zhixin Shu, PhD, CFA
October 2020