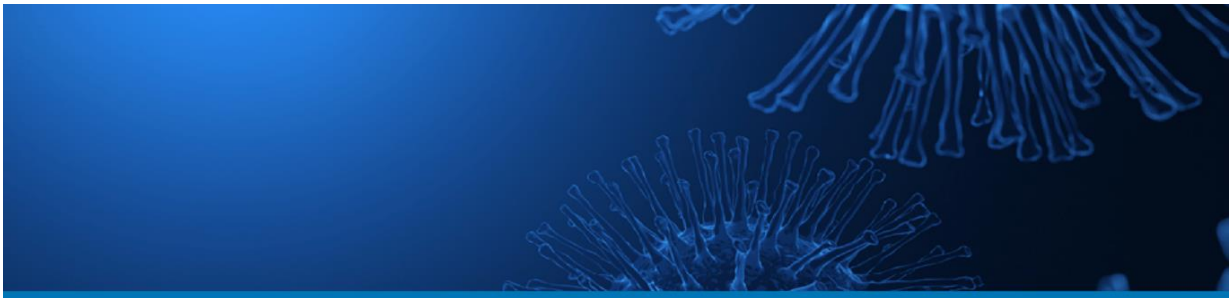

COVID-19
UK Political Analysis

By Tim Hames, Senior Adviser | 24th July, 2020

FTI CONSULTING

Blues in the pink? How the Oxford University vaccine has evolved.

This has been a disturbing week in the struggle against coronavirus internationally. It seems to be close to out of control in parts of the United States. There has been evidence of extensive local second spikes in countries such as Spain, which were hit very hard at the onset of the disease and imposed a rather more comprehensive lockdown than was the case in the United Kingdom. Others such as Australia, which appeared to have dealt with the virus very efficiently during the first wave of infections, are now finding many more new cases having thought that the virus was virtually eradicated. So far the numbers of infections, hospital admissions and deaths in the United Kingdom do not seem to be rising rapidly in response to the lifting of the lockdown, although there have been prominent isolated examples such as in the city of Leicester. All of this makes the search for a vaccine even more important. The story of the week for the virus crisis has been the publication of the results of the first two phases of human testing of the Oxford University vaccine in *The Lancet*. These appear to be very encouraging. How this particular vaccine came to be the front-runner is the focus of this FTI Political Analysis.

EXECUTIVE SUMMARY

- Without a vaccine, a return to truly 'normal' social and economic life is very hard to envisage. Restrictions of some form could last well into next year.

- While there are many vaccine projects being developed around the world, only a few are within striking distance of “phase three” trials on human beings.
- Two of this elite set are based in the UK, namely those associated with Oxford University and Imperial College, London.
- A number of factors, including the early injection of cash from the government and the willingness of Oxford to partner with AstraZeneca, have put the Oxford initiative into the leading spot as confirmed by the results in *The Lancet*.
- In the most optimistic scenario, the vaccine could be deemed ready for mass human deployment within weeks, with manufacturing completed by October and a national vaccination scheme in full swing before the end of 2020.
- Vaccination on this scale would, however, be an immense challenge. It may be necessary in the UK to involve the Army to play a large part in the effort.

Oxford University has an extremely long history, dating back to 1096 according to some sources. For most of that time, it has been associated more with the arts than the sciences. It began as a centre for the study of theology, whereas its counterpart in Cambridge focused on mathematics. The exception to this rule (and the differences between the two institutions on science has declined rapidly in the past two decades) has been medicine. Oxford benefited from huge philanthropic donations to support medical research courtesy of Lord Nuffield in the 1930s and has never looked back.

The timeline of the race for the vaccine (part one).

On January 8, the WHO confirmed that the mystery virus to which it had been alerted on December 31, 2019 had been investigated and identified as a new coronavirus. The next day, by coincidence, Oxford University announced that there would be a new phase one trial of their MERS (Middle East Respiratory Syndrome) vaccine, known as ChAdOx1, in Saudi Arabia. The team that had produced the prospective vaccine was headed by Sarah Gilbert, a brilliant Professor of Vaccinology at the Jenner Institute in Oxford.

That team started work on an entirely different project, a vaccine for coronavirus, 24 hours later. They would be assisted by the fact that Chinese scientists released the full genomic code of the coronavirus about two weeks after that. This enabled the Oxford team to make an early decision as to what sort of vaccine might be applicable. They

settled on a common cold virus found in chimpanzees with a spike glycoprotein, a genetic material extracted from the coronavirus itself. The essential idea was that this combination would, when injected into the body, trick and trigger it into producing antibodies to defend itself and blood-based T-cells. This 'double whammy' is important because antibodies can fade over time whereas T-cells tend to be much more robust.

At about the same time, a team at Imperial College, London, led by Professor Robin Shattock, started work on designing their own vaccine. Meanwhile, the Coalition for Epidemic Preparedness Innovations (CEPI) announced that it would award grants to those who were conducting research into how to stop the virus. On January 24, Matt Hancock, the Secretary of State for Health and Social Care, ordered an acceleration of UK-based trials for a coronavirus vaccine and started to search for money to fund it. He did not want, however, to put all of his proverbial eggs in the domestic basket. So, on February 3, he announced an extra £20 million for CEPI as well. On February 5, the Imperial team had generated its vaccine candidate and five days later would start animal tests with that potential vaccine. Between those two dates, Oxford University (which had already quietly initiated animal tests) named its vaccine contender as ChAdOx1 nCOV-19 and announced an arrangement with Italian manufacturer Advent Srl to produce the first one thousand doses for the initial clinical trials. The race for the vaccine was on.

The timeline of the race for the vaccine (part two).

By March, Oxford had invited donations to its Coronavirus Research Fund, which has turned out to be one of the easier examples of university fundraising in history. It was being reported that it was preparing to begin safety trials of its vaccine on humans as early as the next month. More speculative media stories suggested that further animal trials for the same vaccine would commence at the Public Health England laboratory at Porton Down the following week. On March 24, the Government donated £2.2 million to Oxford to cover the costs of the human trial. On March 14, Imperial College declared that it would be in a position to start human trials in June, if funding were available. It established its COVID-19 Response Fund on March 25 (sixteen days after Oxford had) and the cash came rolling in. By now, it had formally named its vaccine as LMP-nCoVsaRNA.

The Government still did not want to be accused of medical nationalism. Following a virtual G20 summit, Boris Johnson declared that the UK would donate an additional £210 million to global vaccination experiments. This made the UK the largest such supporter in the world (as it still is). There were plenty of potential recipients. There were at least 150 serious institutions looking for a vaccine worldwide. The tally was as high as 205 on one count. They included a couple of interesting American businesses, Moderna and Inovio.

On April 2, a set of scientists at the Commonwealth Scientific and Industrial Research Organisation (CSIRO) began animal tests of their own on the Oxford and Inovio vaccines candidates, to operate in parallel with human tests. A week later, a team operating from the University of Southampton announced their findings that the virus appeared to have "low shielding", potentially making an effective vaccine a more straight-forward exercise.

By now, Oxford were really rolling the dice. On April 11, Professor Gilbert offered an interview with *The Times* in which she stated that the Oxford vaccine could be ready for the public "by September". She also said that she was "80% confident" that the vaccine would prove successful. The next week, Oxford released the information that human trials would start the following week and that the University would aim to have a million doses ready by September. In other words, it was so confident that it was ready to start making the vaccine before human testing was anywhere near completion.

On April 17, ministers also doubled down and launched the UK Government's new Vaccine Taskforce. It would be led by Kate Bingham, a long-time and successful life science venture capitalist. On April 21, Matt Hancock unveiled an extra £20 million for Oxford and another £22.5 million for the Imperial vaccine team. A day later, the first five sites for Oxford's clinical trials were identified. The first human trials of the Oxford virus started on St George's Day (within 48 hours, 'fake news' stories would circulate that the first volunteer to be injected had died). On April 27, rather more accurate preliminary reports emerged that six macaque monkeys who had received the Oxford vaccine in a Montana specialist laboratory had remained healthy for 28 days, even after extremely heavy exposure to coronavirus. On the last day of that month. Oxford University entered into a partnership with AstraZeneca for the development and manufacture of their

vaccine candidate. This was a huge move in that it represented an alliance between the academic and commercial that was and is a relatively rare occurrence.

The timeline of the race for the vaccine (part three).

With human trials in full swing, there was comparative silence from the various teams, though crucially it did emerge on May 14 that all of the monkeys in Montana had developed antibodies. On May 17, Alok Sharma, the Secretary of State for Business, Energy and Industrial Strategy, announced an additional £84 million in government funding to press on with research at Oxford and Imperial with the objective of making 30 million doses available as early as September if the best-case scenario was realised. He also set out the construction of a £38 million 'rapid deployment facility' to allow for the vaccine to be manufactured quickly and at scale. This would churn out vaccines until the opening of the Vaccines Manufacturing and Innovation Centre (VMIC) in Oxfordshire, which was to be fast-tracked by 12 months to open in summer 2021 at an additional cost of £93 million.

AstraZeneca, meanwhile, was clearly enjoying its association with the Oxford project. The CEO had said on television on the day that the deal was revealed that they would know by the end of July whether it would be effective (that might prove optimistic). On May 21, the company claimed that it had the capacity to manufacture a billion doses of Oxford's vaccine candidate. Three days later, the CEO returned to the airwaves to confirm that the UK government had ordered 100 million doses of the Oxford vaccine, the first of which would be ready from September. On June 3 he popped up again, this time to announce that they had already started to manufacture the Oxford vaccine. A day later he was able to reveal that the company could double its manufacturing capacity having reached agreements with the Serum Institute of India and the Bill and Melinda Gates foundation. The day after that a $750 million deal with CEPI also became public.

There were a couple of hitches. There were concerned reports in sections of the media that the Montana monkeys had developed the virus after the trial, although none had suffered damage to their lungs or shown any signs of pneumonia. It fell to Professor

Andrew Pollard of the Oxford team to point out that this was what was supposed to happen. Preventing pneumonia was the primary purpose of the exercise.

Alarm was raised when Professor Adrian Hill from Oxford said in an interview that the virus was abating so quickly in the UK that there was only “a 50% chance” that the vaccine would be successful. A solution to this was soon found: move the trials to places where the virus was still prevalent. An agreement with the Brazilian health regulatory agency was struck to allow Oxford to conduct clinical trials of its vaccine candidate in that country with plans drawn up to seek 2,000 local volunteers. A similar arrangement was later reached to conduct trials in South Africa and the United States. In an interview with LBC, Sir John Bell (from the Oxford team) floated the idea that the entire UK population could be vaccinated by Christmas.

The Imperial College option is not off the table. Last month it announced that it would create a start-up business to distribute its vaccine at low cost in order to side-step the massive pharmaceutical companies. It also started comparatively small-scale human trials (involving 300 people) last month and expects to move on to a much larger trial (6,000 people) in October; last week Professor Shattock stated that their vaccine could be available by the first half of 2021. Last Friday, it announced that the very first trial (which involved only 15 people) had succeeded and a further 105 people were now involved.

This does, however, increasingly look like a Plan B. Oxford is trialling at a much more intense scale. It has mooted that the best-care scenario would be for it to begin deliveries in October. Trials of the vaccine in pigs conducted by the Pirbright Institute suggest that it is at its most effective when administered in two doses, which will slightly complicate the process of implementation. The Chief Scientist at the World Health Organisation has described the Oxford vaccine to be “the leading candidate” and Kate Bingham, chair of the Vaccine Taskforce, told the House of Commons Science and Technology Committee on July 1 that the Oxford project was the best hope of a vaccine this year. Professor Gilbert oozed confidence when she spoke to the same Committee. On Monday this week the reason for her confidence became more obvious, following the

publication of phase one and phase two results in *The Lancet*. The vaccine caused a strong immune response in terms of antibodies and T-cells, and it was safe for humans.

Ministers are still being careful not to have only one horse at the racecourse. On the same day that *The Lancet* article was published, the Business Secretary announced that the government had agreed partnerships with BioNTech/Pfizer and Valneva to secure early access to 90 million doses of their proposed vaccines. This means that the UK has access to multiple different vaccine candidates and the government continues to be the most aggressive in the world in supporting international attempts at vaccine research.

The implications of where the vaccine race stands now.

There are several implications – some plain, others less so – to the narrative that has been set out in this FTI UK Political Analysis (although this week it is closer to FTI Medical Analysis).

The first is that if a vaccine is not found this year it will not be for want of trying. The UK Government has thrown the kitchen sink and a lot of hard cash at a vaccine. Few other governments have been anywhere near as proactive in seeking to discover one early.

The second is that, unless there is something incredibly secret taking place in a laboratory in China, the Oxford vaccine candidate is the most credible contender. This is because the team there had an original idea as to what might work at a very early stage and proved to be fast and flexible in doing whatever it took to move at speeds unknown in medical history. The arrangement with AstraZeneca is a primary example of this. The Ivory Tower is not the natural ally of Big Pharma. Imperial College, London were clearly very uneasy about such an understanding, preferring to attempt to create their own start-up rather than risk being swallowed alive by one of the largest companies in this field. In the fullness of time, we may yet discover that the Imperial vaccine – an audacious medical first which they will continue to develop – is medically superior to the Oxford one. Speed, however, is of the essence here. Betamax was objectively better than

VHS (for those readers of a certain age who can remember these items), but VHS was on the market first. The same may yet transpire with the vaccine.

The third is that there will now be an awfully large number of disappointed people (not least in the Department of Health and Social Care) if the Oxford vaccine falls at the final hurdle. The progress set out in *The Lancet* is astonishing, even for those of us who had to struggle to understand it even partially. It is no longer fanciful to expect many people in the UK to have been vaccinated before the end of this year. Indeed, one could deduce that the Prime Minister's press conference last Friday setting out further means by which the lockdown could be lifted faster and his willingness to speak about a degree of normality "by Christmas" only makes sense if he is privately being briefed that a vaccine is close.

The fourth is that the outstanding element in understanding the Oxford virus is less whether or not in crude terms it will 'work' but how long it will work for. There is a split in the public pronouncements on this between the CEO of AstraZeneca, who last month suggested that it would provide protection for about a year, and Professor Gilbert, who told the House of Commons Science and Technology Committee that she believed that it would offer immunity for several years. There is a huge difference in terms of the practicality of life between an annual jab for (ideally) almost eight billion people across the globe, a jab (or probably two jabs) every five to ten years, and lifetime immunity.

Fifth, it is unlikely that manufacturing the vaccine will prove to be a bottleneck, at least in this country. AstraZeneca is entirely capable for manufacturing enough doses for 70 million people in relatively short order (weeks not months), and indeed has already begun doing so.

Sixth, the real challenge will come in distribution and implementation of vaccination. The vaccine needs to be kept cool; it cannot be simply posted out to people. Vaccinating the entire country will be a vast undertaking, most likely requiring the military in large measure (not least because the rest of the NHS would be totally distracted if it had to complete this task alone, with an adverse effect on conventional patient care). There would also be some tough calls to make ethically and politically. Should it be mandatory, so that we can be confident that the virus has been completely contained? What do we

do about the refuseniks on the vaccine, including those paralysed by fear at the thought of needles entering their bodies (and there is a sizeable section of those in the community)? How about the homeless?

These issues are difficult, but they have at least been contemplated. A key section of the national pandemic plan that ministers inherited for this crisis, although mostly unhelpful because it was predicated on an influenza outbreak of atypical scale, was devoted to how a national influenza vaccination scheme might be executed. It will doubtless have to be amended for contemporary circumstances, but it does exist as an opening blueprint.

Finally there is the danger, if the vaccine does come, of celebrating victory too early. The virus could mutate in a manner that requires the vaccine to change as well and be readministered. There could be future examples of a coronavirus that are different to this one. There will be parts of the planet where it will be extremely hard to run a vaccination programme. Something might sink the Oxford vaccine at the last minute (although it is not easy to think what that might be). In any case, the recommended summer reading to be taken on holidays this year has to be some dense pages of print published this week in *The Lancet*.

Tim Hames
Senior Adviser
Strategic Communications
Tim.Hames@FTIConsulting.com