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Initial COVID-19 vaccine efficacy

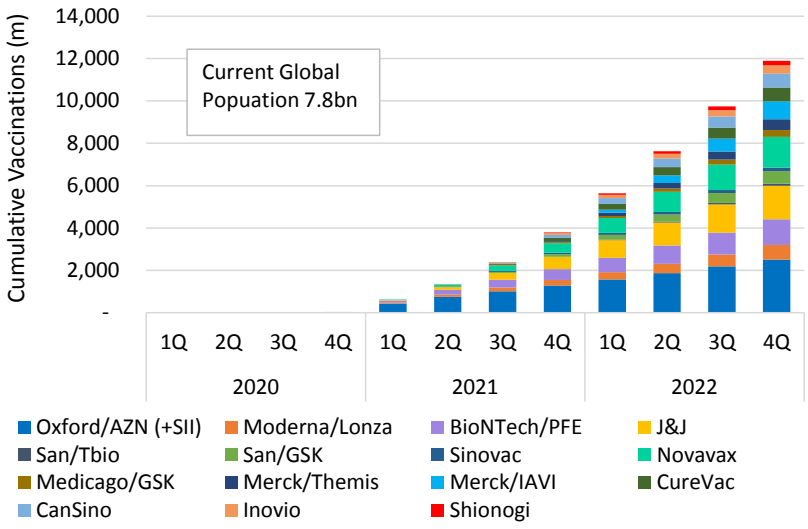
Bio-Pharma Team Q&A on 'back to normal' timelines

Major Pharmaceuticals | Comment

In June 2020 the CS Healthcare Team set out its **'Back to Normal' framework assumptions** based on ongoing COVID-19 therapeutics, diagnostics and vaccines (LINK). Following the publication of the first interim Phase 3 efficacy data from the Pfizer/BioNTech COVID-19 vaccine, we have seen significant interest from specialist and generalist investors on how today's news fits into that framework. **In this report, we aim to answer the most frequent questions we have received**. We also highlight the next key catalysts that we see in COVID-19 vaccine development and raise the key unknowns which are yet to be resolved.

- **How good is the data from Pfizer/BioNTech relative to your expectations?**
- **Manufacturing capacity – how much is there and how quickly can it ramp?** Can we retool other vaccine manufacturing capacity to make the Pfizer vaccine?
- **Are other vaccines now relevant or is this all we need?** What does this tell us about the likely success of other vaccines?
- **How quickly will we get mass vaccination?** What are the logistical challenges?
- **What don't we know about the PFE vaccine and when will we find those answers out?**
- **What are the next key catalysts for broader COVID-19 vaccine development?**
- **Durability of response – the critical unknown in our view**

Figure 1: COVID-19 Vaccine estimated cumulative capacity by patient over time



Source: Company data, Credit Suisse estimates

Research Analysts

European Pharma Team
44 207 888 0304
creditsuisse.pharmateam@credit-suisse.com

Trung Huynh
44 20 7888 2102
trung.huynh@credit-suisse.com

Dominic Lunn
44 20 7883 0471
dominic.lunn@credit-suisse.com

Elizabeth Walton
44 20 7883 9767
elizabeth.walton@credit-suisse.com

Jo Walton
44 20 7888 0304
jo.walton@credit-suisse.com

Matthew Weston PhD
44 20 7888 3690
matthew.weston@credit-suisse.com

Evan Seigerman
212 325 4463
evan.seigerman@credit-suisse.com

Specialist Sales - Philip Gestrin
44 20 7888 1000
philip.gestrin@credit-suisse.com

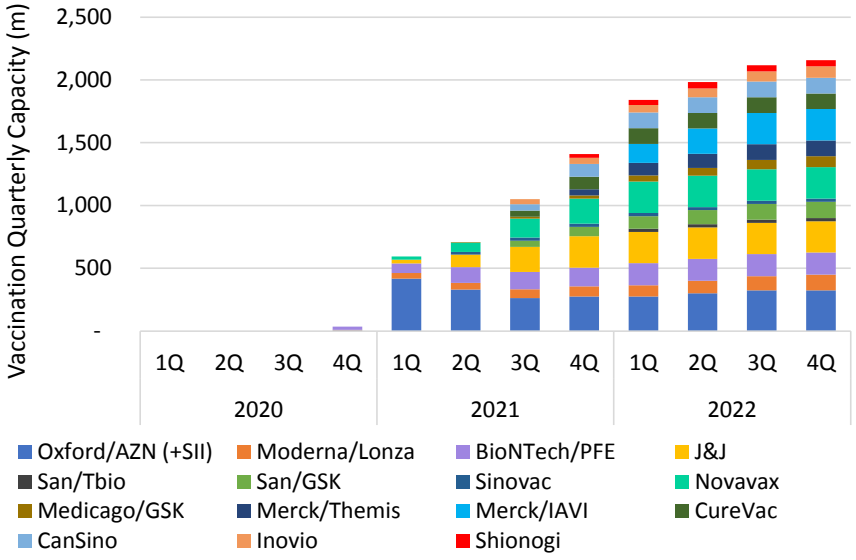
How good is the data from Pfizer/BioNTech relative to your expectations?

- The interim Phase 3 data published yesterday highlights a 90%+ efficacy of the Pfizer/BioNTech COVID-19 vaccine. We see this as the best possible outcome for an interim readout relative to our and government expectations.
- The FDA had stated that it was prepared to consider a vaccine with >50% efficacy. The NIH has more recently suggested that a hurdle of 60%+ was more appropriate. Within that context 90%+ is as good as you can get!
- The vaccine also gives protection 7 days after the second vaccine dose. This highlights in our view a rapid and deep response, although duration of protection is yet unknown.
- We also see the 90%+ efficacy as a very important catalyst for encouraging broad public vaccination. Unlike most vaccination schedules (which happen semi-automatically during childhood), COVID vaccination will require the general public to decide that they want to be treated. The fact that being vaccinated gives 90%+ personal protection is very important in this context, in our view. A 60% efficacy vaccine would have been great for society and to build herd immunity, but would not guarantee protection of the individual. Today's data makes a vaccination decision very much one of personal protection.

Manufacturing capacity – how much is there and how quickly can it ramp?

- Pfizer has announced that it can produce 50 million doses by year-end 2020 and up to 1.3 billion doses in 2021. Recall each person requires two doses of vaccine for protection.
- The 1.3 billion target is in line with prior comments from the company.
- The 50 million doses in 2020 is actually lower than previous target (100 million).
- We assume a broadly linear ramp in manufacturing capacity over 2021.
- BioNTech recently acquired a ready-built facility from Novartis in Marburg Germany with a capacity for 750 million doses in due course. Some fill/finish will be provided by Siegfried.

Figure 2: COVID-19 vaccine supply by company (per patient)



Source: Company data, Credit Suisse estimates

Can we retool other vaccine manufacturing capacity to make the Pfizer vaccine?

- Multiple vaccine technologies are being employed to develop COVID-19 vaccines. The Pfizer/BioNTech vaccine uses an mRNA approach. Similar technology is being used by others including Moderna and Sanofi/Translate Bio.
- Theoretically, elements of the manufacturing capacity for these vaccines could be redeployed to make more PFE vaccine, in our view.
- However we only expect this to become a relevant consideration if these other vaccines fail to show meaningful efficacy in due course.
- While Moderna's manufacturing relationship with Lonza is a 10-year deal across a portfolio of mRNA vaccines, we would expect short term capacity that has been slated to be used for the Moderna vaccine to be redirected to the Pfizer vaccine if the Pfizer vaccine efficacy proves to be unique, and if Pfizer is unable to supply demand.
- Other vaccine technologies (viral vector/traditional protein antigen) cannot be retooled to manufacture the PFE mRNA vaccine.
- However one of the biggest bottlenecks for vaccine distribution is expected to be fill/finish into vials. While this will have been contracted by each of the leading vaccine players today, we expect that this will be appropriated/contracted by governments for the successful vaccines if some are seen to fail.

How quickly will we get mass vaccination? What are the logistical challenges?

- We expect that the first doses will be reserved to high risk patients (elderly/immune-compromised) and to workers in high-exposure jobs (eg. healthcare workers, carers).
- There are still very substantial hurdles to mass vaccination. The first is clearly supply (see above). Beyond that, the Pfizer/BioNTech vaccine requires a very low -70°c cold chain for distribution. This is not something that is widely used in clinical practice today and will take significant logistics to expedite.
- Pfizer, the CDC and others have been working for some time on this logistical issues. This includes a -70°c bulk supply chain between cities within the US and specific cooled packaging ("thermal shippers") to allow smaller deliveries to the regions.
- We believe that a low temperature supply chain will be relatively simple in order to reach healthcare workers (vaccinate in hospital when at work) and in large care homes (mobile vaccination units with appropriate logistics).
- Mass vaccination logistics will be much more challenging beyond these settings. However, if this proves to be the only vaccine available then there will be considerable political and economic will to find solutions to this challenge.
- We do not see the Pfizer/BioNTech technology as being particularly appropriate for less developed economies where the logistics of cold-chain distribution will be much more challenging.

When can we stop wearing masks and isolating?

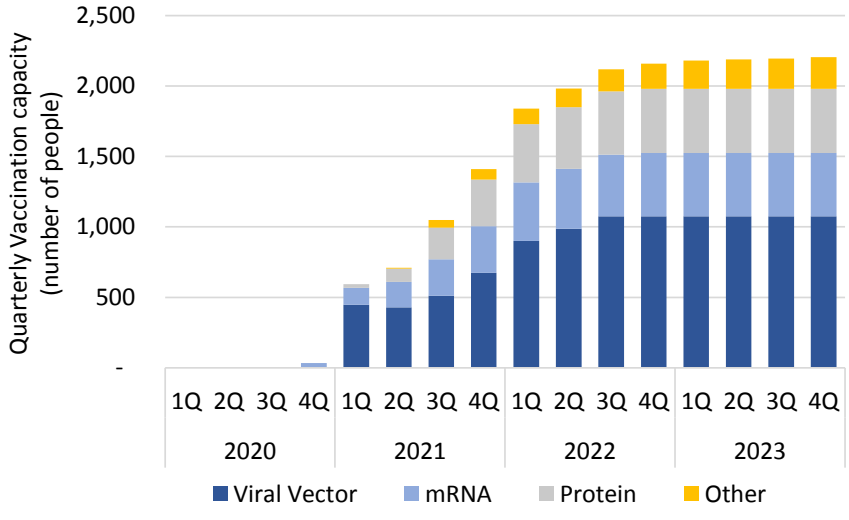
- While the news from Pfizer/BioNTech is clearly extremely encouraging, we expect very clear public notes of caution from politicians in the coming days.

- This reflects the lack of final efficacy/safety data as well as challenges of supply and the logistics of mass vaccination which mean that a broad deployment of vaccine is unlikely until 2H21 at the earliest.
- Given the current ramp in global infections, the risk that people drop their guard and ignore normal protection (masks/hand washing) will be a huge concern to public health officials.
- Any move to relax precautions will likely lead to a rapid spike in virus cases which would risk overwhelming the hospital system during the busy winter season. Vaccines alone are not enough to stop the pandemic, and we need to see further progress on both diagnostics (there are a greater amount of less invasive, and quicker technologies being rolled out) and antibody cocktails that are in development to lower the severity of illness post exposure. COVID therapeutic antibodies could potentially provide protection for close contacts of infected patients as they provide almost immediate protection (days), where a vaccine would be no use given the time it takes to develop an immune response (weeks).

Are other vaccines still relevant or is this all we need?

- The majority of vaccines in development have broadly all targeted the same viral fragment to induce the immune response. As such, today's PFE news provides hope that others have a good chance of success and hopefully with a similar high level of efficacy.
- However, we see it as critical that other vaccines are successful to address the challenges of both global supply and the logistics of -70°c cold chain distribution. We note that Moderna's mRNA vaccine needs to be stored at -20°c.
- The viral vector technology approach (AZN/Oxford, J&J, MRK) was specifically chosen because of the high degree of scalability of manufacture. We estimate that c.55% of global planned COVID-19 vaccine capacity (assuming all key players are successful) is based on viral vector technology. Protein-based technologies represent a further c.25% of 2021E capacity.
- Non-mRNA based technologies (viral vector and protein fragment) require more normal cold chain logistics of 2-8°c (a normal household fridge).
- We see a broad success across multiple vaccine platforms as critical to the global response to COVID-19 and an ability to really achieve 'back not normal' for the global economy.

Figure 3: COVID-19 vaccine supply by vaccine technology (per patient)



Source: Company data, Credit Suisse estimates

What don't we know and what are the next catalysts?

We see four key incremental catalysts to address before year-end 2020:

- Before it can file for Emergency Use Authorisation, Pfizer/BioNTech need to present **interim safety data**. This is expected during "the 3rd week in November". To provide some reassurance, Pfizer today highlighted that no major safety issues have been observed to date.
- **Final Phase 3 efficacy data** from the Pfizer/BioNTech program will be reported when 164 events have been reached. Bill Gruber, SVP Vaccine Research & Development at Pfizer is reported as saying this could be reached in early December 2020 based on the current trajectory of COVID infections (source: Reuters). Given the very strong data reported at this interim read, we see this datapoint as offering modest downside risk. The PFE trials are known to have broadened out recruitment over time to include harder to treat elderly and immune-compromised patients. We see modest headline risk if the efficacy slips from the 90%+ level but still note that it is likely to far-exceed the 50-60% efficacy level targeted by FDA/NIH.
- **Interim efficacy data from the Moderna mRNA COVID-19 vaccine program.** At the end of October 2020, Moderna stated that interim data from its Phase 3 vaccine trial (also using an mRNA technology) could be available in November 2020. The independent data monitoring committee is expected to conduct an interim review in this timeframe. Moderna has said that it expects to be able to produce 20 million doses of its vaccine by YE 2020 and between 500 million and 1 billion in 2021. Moderna believes that its mRNA vaccine can be distributed at -20'C (a normal household freezer) which would significantly simplify some of the cold-chain logistics.
- **Efficacy data from the AZN/Oxford COVID-19 vaccine program.** Originally seen as one of the front-runners, the AZN/Oxford program has been delayed by a number of safety observations during the studies. Following full investigations by the independent data monitoring committee, the trials have all been allowed to resume. Data from the Phase 3 AZN trials are expected before year end 2020. This data will be based on the ex US cohorts of patients (Brazil, South Africa and the UK) with a US cohort currently enrolling. We assume ex US timelines for AZN will be on a par with others, but we note that the FDA may wait for a US cohort before considering the vaccine.

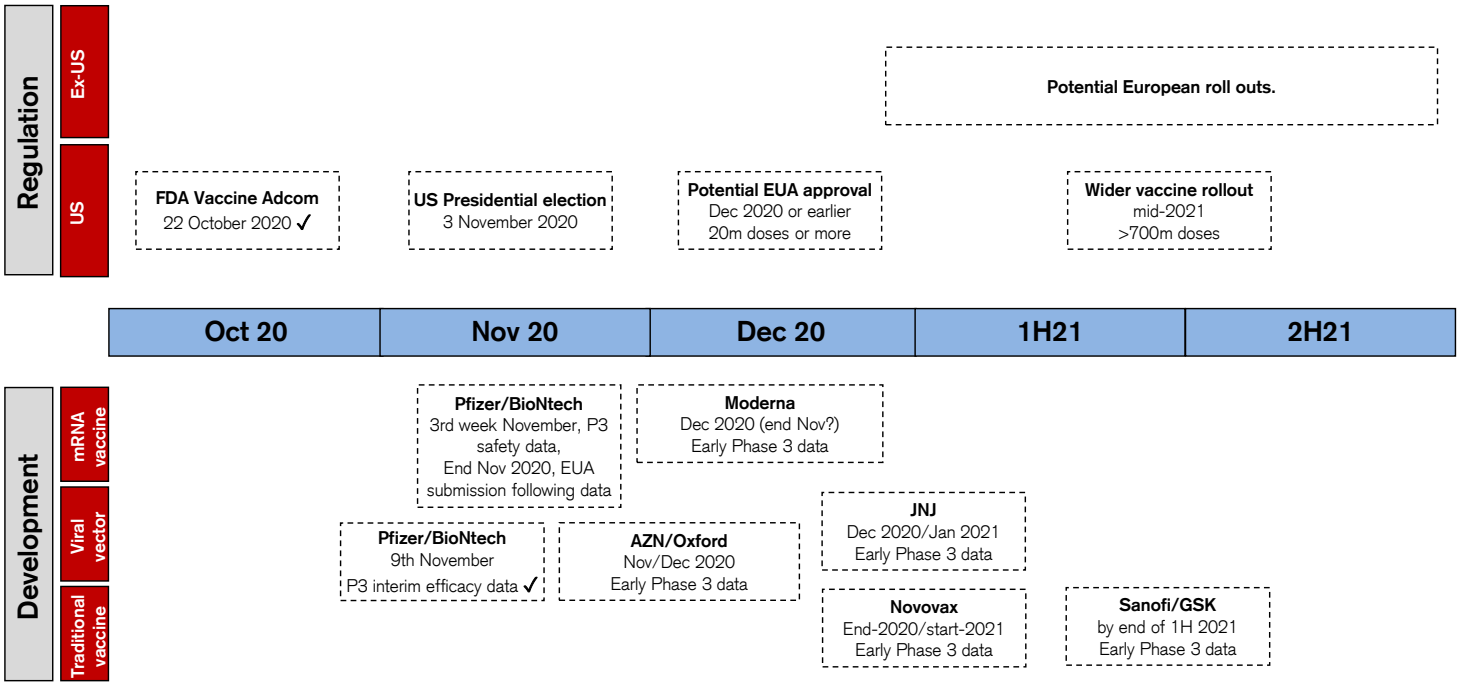
Durability of response – the critical unknown for 'back to normal' timing in our view

- Despite the very positive stock market reaction to the positive efficacy data from Pfizer/BioNTech's vaccine, one key data point is not yet known and will be unclear for some time: How long will protection from the vaccination last?
- Normally durability of protection data would be available before a vaccine was filed. However, the accelerated development during the pandemic means that this will only become clear in due course as patients from the clinical trials are monitored. This will likely come AFTER Emergency Use Authorisation is granted and broad vaccination has begun.
- Durability of response to vaccines can range from a lifetime (key pediatric vaccines like measles/mumps) and one annual season (influenza). Where COVID-19 fits in this range is unknown.
- We do know that the natural antibody immunity from a COVID-19 infection does not appear to last long in people, especially those with only mild symptoms.
- However, other layers of immunity can come from other parts of the immune system (e.g. T cell response) which could provide significant protection beyond that provided by antibodies.

- Only time will tell how long the duration of response to COVID-vaccines will be.
- Clearly, if the duration is only 1-2 years then the logistical challenge of global mass repeat vaccination will raise real issues with a sustained move to 'back to normal'.

COVID vaccine timeline

Figure 4: COVID vaccine timeline



Source: Company data, Credit Suisse estimates

Companies Mentioned *(Price as of 09-Nov-2020)*
AstraZeneca (AZN.L, 8301.0p)
CureVac (CVAC.OQ, $54.66)
GlaxoSmithKline plc (GSK.L, 1428.2p)
Johnson & Johnson (JNJ.N, $146.08)
Lonza (LONN.S, SFr620.0)
Sanofi (SASY.PA, €84.93)
Shionogi (4507.T, ¥5,600)
Siegfried Holg (SFZN.S, SFr639.0)

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Credit Suisse International European Pharma Team ; Trung Huynh ; Dominic Lunn ; Elizabeth Walton ; Jo Walton ; Matthew Weston PhD
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