

Neuberger Berman Equity Research Team

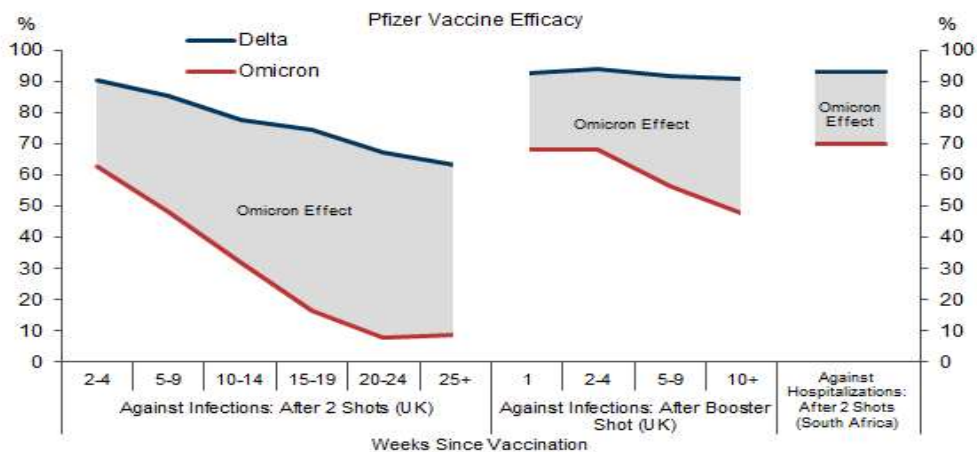
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U.S. COVID-19 Update: Moving Past the Omicron 'Bump' as the Endemic Phase Unfolds

*Re-reading our COVID-19 update from last month, we were struck by speed with which BA.2 arrived in the U.S. and rapidly spread through the country, gaining a foothold in the Northeast, which has been the virus *modus operandi* for some time now. While we wrote that new cases were ticking "down to about 40,000 per day in the U.S." last month, today some are sounding alarm bells at the April 18th update of some 35,000 new cases per day in the U.S. versus a low of about 20,000 three weeks ago.*

In our view, tracking new cases is less helpful given the level of at-home/antigen testing, most of which is not captured in numbers from the Centers for Disease Control. While admittedly testing positivity rates are back to about 5%, we note that hospitalizations and ICU bed occupancy for COVID-19 are thankfully still declining. This is indicative of a less virulent strain in BA.2 or broader baseline protection of the population from severe COVID-19, or a combination of both. Below, we attempt to answer key questions we have been getting regarding what's next, how are we thinking about the future and whether we can erase the word "COVID-19" from our vocabulary. (The answer to this last question is "probably never.")

EFFICACY OF VACCINES OVER TIME AND AGAINST VARIANTS (PFIZER)



Source: UKHSA, Discovery South Africa, Goldman Sachs Global Investment Research As of April 20, 2022

What could be the next SARS-CoV2 version? BA2.12.1? BA.3? 'Deltacron'? or Pi?

We are not so naïve as to think that this virus is done with us yet, given that U.S. vaccinations rates/boosters are respectable but nowhere close to herd immunity levels. Still, if you rationally approximate the level of baseline infection across the U.S. population and those with hybrid immunity, and consider the 80%+ vaccination rates as measured by first dose, you could reasonably look at the latest data on hospitalizations and argue for longer-term protection from severe COVID-19 driven, not by neutralizing antibody levels, but by adaptive immunity (B and T cells). If this is correct, most in the developed world will likely be able to handle a BA2.12.1/BA.3 subvariant or a combination of prior variants, which we have not-so-cleverly named "Deltacron." Regarding a new variant, SARS-CoV2 has shown an astounding ability to tolerate more mutations in the spike regions than most models would have predicted, so we are not yet ruling out another variant of concern (Pi, next up in the Greek alphabet). Wastewater detection rates are on the rise, which has served as a leading indicator to date of an inflection in cases and/or new variants. However, note that Omicron appears to be evolving more through genetic drift, a la influenza, rather than the more drastic, mutational profile of earlier variants.

What's new on the vaccination and treatment front?

- Data released earlier this week from Arcturus Therapeutics' self-amplifying mRNA vaccine candidate (ARCT-154) was encouraging but early, with 95% protection from severe COVID-19 versus a placebo at day 56 post-dosing and 55% reduction of infection versus all strains, the former on par with mRNA vaccines.
- The European Union approved AZN's Evushield in late March for pre-exposure prophylaxis in high-risk individuals over 12 years of age with utility retained against Omicron variants including BA.2 with a focus on the immunocompromised community.
- Data from both PFE and mRNA vaccines in kids under 5 years of age remains mixed, in our view.
- Moderna's bivalent vaccine, mRNA-1273.211 (ancestral Wuhan strain and Beta variant), suggested better protection from severe COVID-19 versus most strains tested (ancestral, Beta, Delta and Omicron) relative to the original vaccine, mRNA1273, as measured by neutralizing antibody titer data released on April 20.
- Enanta's EDP-235 oral antiviral has moved into a phase-one study, should report data in the second half of the year; once-daily dosing convenience could drive uptake, if successful.
- In disappointing news, Shionogi's oral antiviral showed robust viral lowering data but safety data remains an open question versus PFE's Paxlovid.

Up next is bivalent mRNA vaccine data targeting Delta/Omicron from Moderna, with data expected in late summer 2022, in time for fall boosters, as well as detailed results from a study looking at coinfection with SARS-CoV2 and either influenza or RSV with respect to hospitalization and death.

What about research on long COVID-19?

We have often pondered where the world would be if we had not entered lockdowns at the first surge in 2020, a la Sweden. In those assessments, we typically supported the lockdowns, considering that protection from severe COVID-19 was unavailable for younger adults and children at the time, and we had no idea how severe COVID-19 would manifest in younger age cohorts. Today, we have ample data that supports a critical view of China's zero-tolerance strategy, specifically emerging data on hybrid immunity affording broader immune protection from severe COVID-19 than vaccination or infection alone, and that the unvaccinated are still at higher risk of experiencing a more severe case of COVID-19 versus the vaccinated and boosted. However, we do not recommend "getting infected with Omicron BA.2" as a means of future protection, as predicting who will suffer from long COVID-19 remains a mystery—an area of research we think is mission-critical at this juncture. The debate regarding the driving factors of long COVID-19 has been narrowed to three buckets: autoimmunity post-infection, chronic inflammation and/or viral persistence. However, we are somewhat frustrated on the lack of broader studies, given ample databases, and think testing current therapies in these patients should become a focus, while evaluation of long COVID-19 patient samples for biomarkers is an area worth undertaking.

We close this note with our views on the status of the endemic phase:

- Now that baseball season is in full swing, we think we are in the third or fourth inning.
- Masking should be optional as masks can still offer an individual some protection in a room or airplane of unmasked.
- We believe most people are "over it," and take comfort in knowing Paxlovid is there for them should the need arise in the future, versus opting for a fourth booster with the original vaccine.
- We await bivalent ancestral/Omicron or Delta/Omicron vaccine data as the most logical next booster, if needed.
- We are looking forward to a COVID-low summer.
- We hope that antibody-dependent enhancement never becomes a concept we have to explain, as it could derail my view of SARS-CoV2 variant X becoming a simple nuisance versus the next crisis!

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For more information on COVID-19, please refer to the Center for Disease Control and Prevention at [cdc.gov](https://www.cdc.gov).

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