

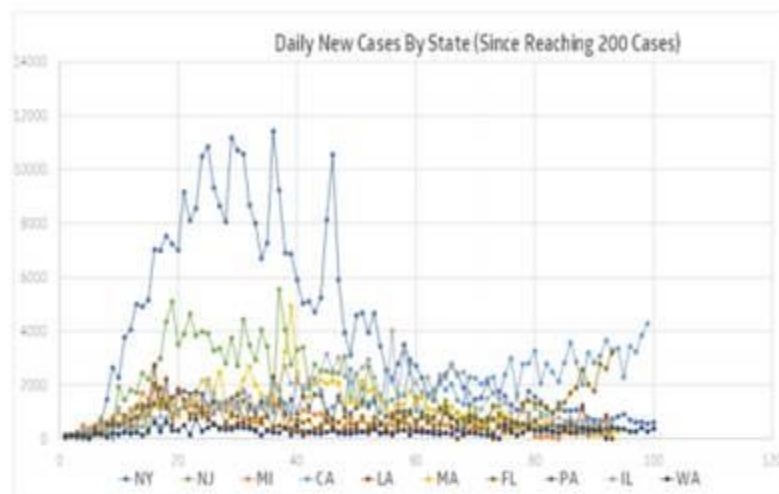
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Covid-19 Update: Second Wave or Lingering Virus?

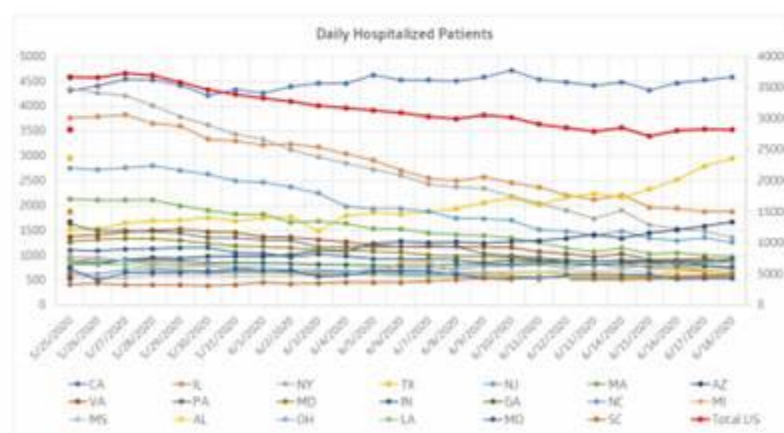
Is this a second wave or a virus that may linger for the foreseeable future? In our view, the latter seems most likely, but we are now better prepared for the fight.

With the outbreak spreading across the Southern Hemisphere (Brazil, Chile hotspots, etc.), SARS-CoV2 (the virus that causes the COVID-19 disease) has not left the Northern Hemisphere, disappointing some who had hoped for positive trends with the approach of warmer weather and more outside activity. Rising cases in states including Florida, Texas, Arizona, South Carolina and California should not come as a shock given the early reopenings in Florida and Texas, more testing across the U.S. and the growing frustration of those “locked down” for three months. We are not downplaying the bump in new U.S. cases (about 28,000 day/day up from the recent seven-day moving average of about 21,000), but note that U.S. hospitalization rates are stable despite spikes in Texas and California. Interestingly, the average age of those testing positive has declined, suggesting that younger individuals are taking more risk as openings proceed. To illustrate, the charts below show daily new cases and hospitalizations across selected states.



Source: JHU CSSE, Cowen and Company

US Hospitalizations Are Stable Overall But Are On The Rise In Some States

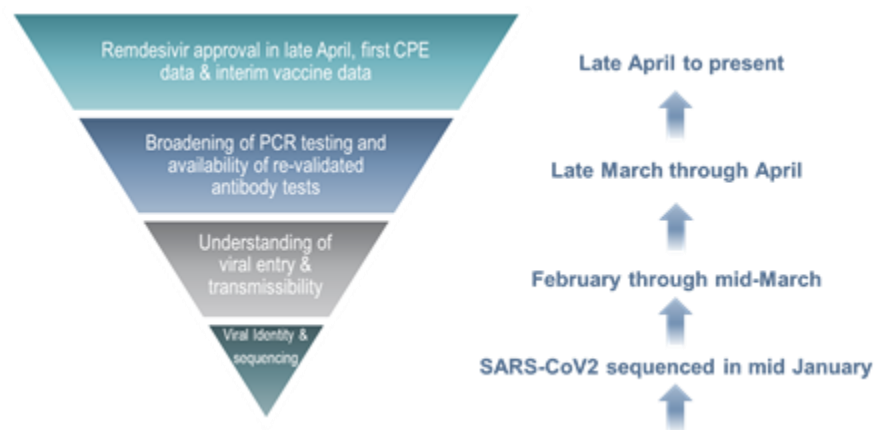


Source: The COVID Tracking Project, Cowen and Company

Reasons We Are Better Prepared

Why do I think we are better prepared for a possible second wave? The inverted pyramid below illustrates how our knowledge base of the virus has exploded since January/February, including:

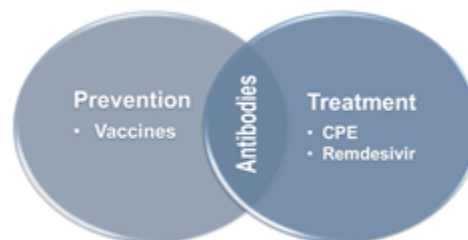
- A deep understanding of the molecular characteristics of SARS-CoV2, including sequencing over 4,300 genomes of the virus from around the world, which suggests that the East Coast strain closely resembles that affecting the EU versus the West Coast of the U.S. which is more akin to the original Wuhan, China strain.
- Detailed knowledge of the mechanism of action for viral entry into human cells via the spike protein and why it appears to be the best and most appropriate target for vaccine development. New data shows that mutations in this region of the virus occur mostly in the non-translational region and hence have limited if any impact to recombinant antibody programs as well as vaccines.
- Additionally, substantially increased viral testing has increased to roughly 480k – 500k per day followed by rapid notification and, importantly, contact tracing, the latter of which was non-existent in March.
- Availability of reliable antibody tests post FDA re-validation after the flooding of the market with inferior, unreliable tests (27 tests pulled from the market to date), which can help us understand the baseline infection rates to help foster herd immunity.
- At least approximately 12 – 15% of the population testing positive for baseline antibodies against SARS-CoV2 to date versus zero in late February, although their duration remains an open question.
- Finally, the Emergency Use Authorization of Remdesivir to aid in reducing the length of hospitalization stays and the possibility that it could impact survival; intriguing, unpublished data on the utility of generic steroids in reducing death in severe COVID-19 patients; and positive interim data from the first vaccine study about three weeks ago.



Source: Neuberger Berman, FDA.gov as of June 9, 2020

Updates on Treatments and Vaccines

The Venn diagram below highlights the intersection of preventative measures such as vaccines and treatment of COVID-19, with recombinant antibodies in the overlapping area, hinting at our view that antibodies may be used as both treatments and as prophylactics as a bridge to vaccines. Why do we like the recombinant antibody programs in development?



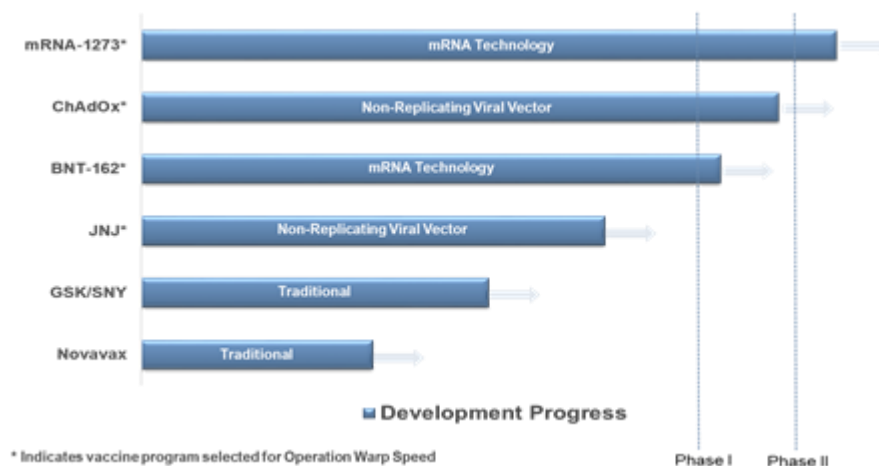
Source: Neuberger Berman, FDA.gov as of June 9, 2020

- They mimic CPE (taking plasma from COVID survivors and reinfusing it into sick people with the idea that antibodies formed naturally in the recovered patient will passively transfer to the severe COVID patient).
- Data to date has been largely encouraging.
- Generally, antibodies act quickly, have a vast safety database as a class of therapies, are straightforward to manufacture and have worked in addressing Ebola.
- Risks include a need to deliver two or three antibodies in one infusion, high costs to manufacture and the fact that they are IV-infused, which could limit use.
- From a timing perspective, studies are expected to start providing data in late August/early fall, moderately ahead of vaccine data.
- Players include Regeneron, Amgen, Eli Lilly, Vir Biotech and Glaxo Smith Kline, to name those who report to be furthest along.

Vaccines Progress to Date

Regarding vaccines, the swimmer plot below shows the various programs we are most optimistic about, as well as progress to date, with lines out furthest to the right moving in phase II.

- Moderna's mRNA vaccine, mRNA-1273, which reported encouraging interim phase I data about three weeks ago is currently in phase II, enrolling a 600-subject study with 300 subjects aged 18 – 55 years and 300 older subjects (over 55 years).
- The non-replicating viral vector technology employed by Oxford University and partner AZN reported interesting non-human primate data showing protection of vaccinated animals from a live SARS-CoV2 challenge, and now has moved into phase II human trials, although we still have not seen the phase I data.
- Pfizer's mRNA vaccine program with BioNtech is a bit behind Moderna's, however they have taken a "multiple shots on goal" approach, running four distinct vaccines in parallel.
- JNJ's non-replicating viral vector program is expected to begin clinical trials in late summer with GSK/SNY's to follow, the latter with traditional protein vaccine technology, representing a low-risk strategy, though the one with the longest lead times on manufacturing.



Source: Neuberger Berman as of June 9, 2020

Notice the asterisks next to several vaccines on this chart, which indicate selection for the Trump administration's Operation Warp Speed, whose inclusion qualifies programs for government funding, assistance in running the phase III trials and manufacturing and procurement aid, and ultimately distribution for those who choose to receive a vaccine upon emergency-use authorization despite limited safety data.

Prepare for Outbreak Clusters

In summary, I believe the market needs to prepare itself for clusters of outbreaks across the U.S. as the reopening progresses. We are carefully watching hospitalization, which appear stable for the most part, outside of a concerning situation in Arizona with roughly 84% of ICU occupancy worrisome, if true, as well as ICU issues emerging in Florida and California. Still, assessing the re-opening metrics set by most states, we think the time is right to move forward, although we cannot stress enough the importance of masks, social distancing, testing, immediate notification and, most importantly, contact tracing to ring-fence clusters when they occur. Finally, with

the average age of COVID-19 infected patients declining, we would expect more relatively mild cases, which could aid in the percent of the population with some form of immunity, although this remains to be seen. In terms of vaccine efficacy expectations, we would set the bar around 60% or higher, provided that data suggests at least 15% to 20% of the population has neutralizing antibodies. However, we note that while the odds of completely wiping out SARS-CoV2 are low with the vaccines currently in development, COVID-19 may be turned into more of a bad cold, like the other four coronaviruses that have been circulating in the U.S. since the early 2000s.

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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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