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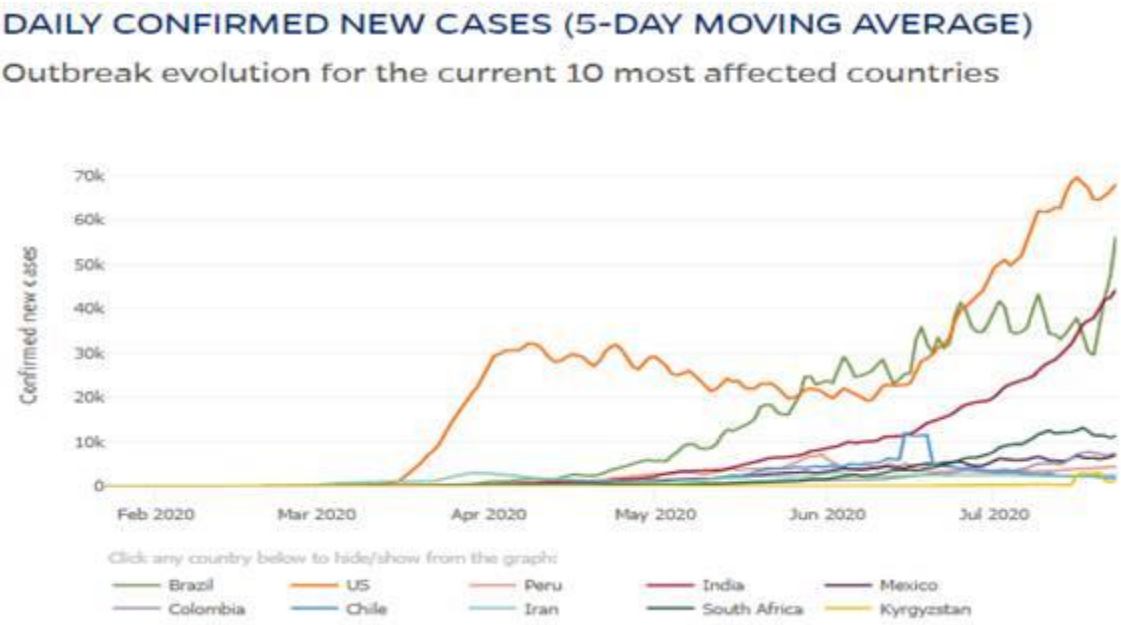
COVID -19 Update: Latin American Surge; U.S. Struggles to Regain Control

Latin America cases are surging, and could possibly overtake those in the United States. However, the U.S. may need more decisive action with time running out to regain control of the outbreak before fall.

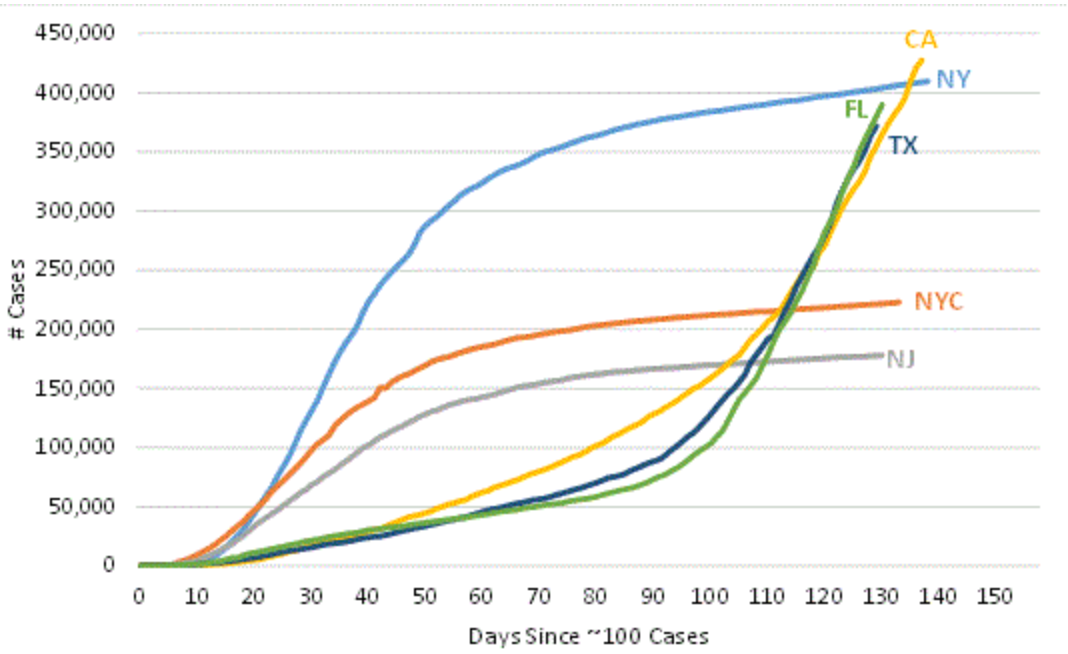
The chart below supports the five-day moving average of confirmed new COVID-19 cases, with the outbreak ramping up in Latin American countries as well as Russia, India and Iran. While Europe appears to be stabilizing, we are watching Spain and the U.K. closely as clusters of outbreaks have led to reintroduction of control measures in the former, while the latter has the unwanted distinction of one of the highest case fatality rates in the world.



Source: Johns Hopkins COVID tracker, as of July 24, 2020.

The U.S. can't seem to get back into the plateau phase as California overtakes New York with the dubious distinction of the most confirmed cases at more than 426,000. Unfortunately, Florida and possibly Texas may be the next states to rise in the SARS-CoV2 (the virus that causes the COVID-19 disease) infection rankings above New York's roughly 409,000, supported in the graph below. The Southeast and Texas show no signs of slowing, in our view, despite hospitalization rates that are concerning yet not alarming, and California's outbreak is clustered in the Los Angeles/San Diego regions, while San Francisco, despite its population density, is holding steady at just under 6,000 cases. Interestingly, the SARS-CoV2 positive testing rate in several states has surpassed that of New York, with Arizona's rate of 18.6%, Florida's 12.14% and Texas at 11.4%, and with California's rate a low of 6.3%, close to New York's 7.6% cumulative testing rate, with a new positive case rate of 1.1% for New York.

Number of Cases, Days Since ~100 Cases



Source: JPMorgan research note, July 24, 2020.

With the pandemic raging on globally, advances in treatments and vaccines are tantamount to society beginning to think about when normalcy can become a reality; the past few days have given us encouraging (yet early) news on several vaccine programs, three of which are now in or about to start large 30,000-patient phase III studies.

Vaccine updates encouraging. Over the past week or so, data from various SARS-CoV2 vaccine studies were reported. The good news is that all three vaccine candidates to date across two distinct technologies reported to have produced neutralizing antibody responses at or above that achieved naturally by patients recovering from COVID-19, along with variable levels of T-cell responses, the latter critical for long-term protection against future infection. Without going into deep scientific analysis in this note, our analysis suggest that several vaccines may be available by year-end 2020 with varying levels of efficacy that could address the heterogeneous global population. I would summarize the data to-date as "so far so good," but keep a close eye on waning antibody responses, which may not prove concerning should memory T-cell and B-cell response seen to date hold true in larger phase III studies. The updates below focus on Moderna, Pfizer/BioNTech and Astra Zeneca's efforts given data releases, but we remind all that Johnson & Johnson's program is expected to enter the clinic any day now, and could potentially place the bar for efficacy above the FDA-mandated 50% at 70 – 80% effectiveness, a show of confidence in their non-replicating viral vector approach, a la Oxford University/AstraZeneca's. J&J has committed to over one billion doses by the end of 2021, with preclinical animal data publication expected in late August for its Ad26-CoV2 vaccine.

- **mRNA based vaccine updates from Moderna and Pfizer/BioNtech**
  - Moderna's phase I mRNA1273 vaccine study was published in the New England Journal of Medicine (NEJM) on July 15 with complete datasets on the 45 healthy subjects versus the 25 first reported on May 18. The data was impressive, in our view, on the level of neutralizing antibodies generated, at titers >4x that of convalescent plasma used to treat severe COVID-19 with some success, a good indicator of eventual vaccine efficacy. That said, the duration of these antibodies remains an open question with levels trailing off between day 43 and 57, which suggests to us that T-cell responses are key to durable protection against SARS-CoV2. Fortunately, mRNA1273 displayed such responses, although skewed to a specific subtype. The phase III COVE study in 30,000 subjects has begun this week and will likely focus on the prevention of symptomatic disease, a lower bar than prevention from infection. On the manufacturing front, Moderna has committed to ~500mm doses by year-end, ramping to over one billion doses per year beginning in mid-2021. The U.S.

government has earmarked the first 300mm doses from Moderna for its population should the vaccine prove efficacious and receive approval from the FDA.

- Pfizer and partner BioNtech announced data from the German phase I study of BNT-162b1, with results largely in line with that reported out of the U.S. study, demonstrating significant neutralizing antibody production as well as broad T-cell responses. The latter are key, in our view, to producing what is known as an immune memory response, critical given emerging data that durability of antibody responses are fairly short, waning around two to three months after natural infection/recovery from COVID-19 as well as to-date in vaccine studies. On the manufacturing front, Pfizer/BioNtech has committed to ~100mm doses by end of 2020, ramping to >1.3 billion doses by the end of 2021 and announced the U.S. government purchase of 100mm doses at a price of $19.50 per dose (~$40 per person as two doses are needed) should BNT-162b1 receive FDA approval. This order could include an incremental 500mm doses at an undisclosed price in 2021. The U.K. government also inked a deal for this vaccine, agreeing to purchase 90mm doses, pending European/U.K. regulatory approval (but at an undisclosed price).

- **Non-replicating viral vector vaccine technology update from Oxford University with partner AstraZeneca**
  - Oxford University/Jenner Institute and partner Astra Zeneca reported interim phase I/II vaccine data for AZD1222, also called ChadOxSARS-CoV2, published in the Lancet journal. The data suggests that efficacy was similar to the Pfizer/BioNtech and Moderna mentioned above, but demonstrated a lower neutralizing antibody response (with all the caveats of cross-trial comparisons) when compared to the mRNA based vaccine strategies, although robust T-cell response in 100% of subjects was reported. AZN1222 is entering last-stage studies in the U.K., Brazil and South Africa, hotspots for SARS-CoV2 infection, with their goal of getting efficacy data faster versus regions where the outbreak is largely under control (i.e., South Korea, Italy, etc.). Additionally, AZN has signed deals with the U.K. government as well as the Serum Institute of India, the latter to provide one billion doses to low- to middle-income countries, with 400mm doses produced by year's end.

Treatment updates: Alternative treatments beyond Remdesivir, recombinant antibody cocktails and other antivirals (which released no new information over the past few weeks), include interesting data on heparin (generic drug) and an inhaled formulation of interferon beta called SNG-001.

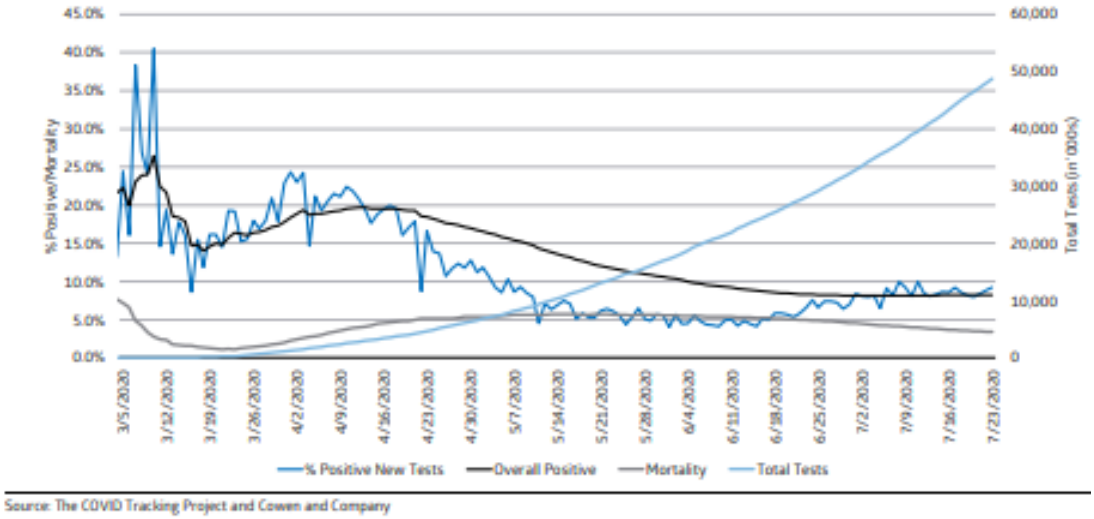
- Regarding heparin, preclinical data suggests that this blood clot prevention drug actually binds tightly to SARS-CoV2 and potentially inhibits its entry into cells. While currently an injected drug, researchers are working on an inhaled version of heparin (as well as nebulized) in animal models to determine if it is worth moving into human trials in the near term.

- Data from a placebo-controlled, double-blind study of an inhaled version of interferon beta called SNG-001 demonstrated a 79% reduction in risk of developing severe COVID-19 disease in patients that had developed symptoms ~9.7 days before treatment as well as a reduction in mean time to hospital discharge of three days (from nine days to six days), in the range of that shown by approved Remdesivir and presumably with a wider window from first symptoms.

With regard to PCR testing for the virus, the U.S. has tested nearly 49mm individuals to date, the most of any country, with a positivity rate that has unfortunately recently ticked higher to >9%, with new positive case rates driving that number higher in hotspots such as Texas, Florida and California.

Importantly, states that have the outbreak under control are tracking at new case positivity rates of ~1%, as reported in New York and New Jersey. We are keenly focused on improved point-of-care tests beyond the ~85% sensitivity of current offerings as well as point-of-care tests capable of detecting influenza and SARS-CoV2 simultaneously, or so called "flu-vid" tests, with commitments out of Danaher's Cepheid platform, Roche diagnostic's lateral flow version in development and Abbott and Becton Dickenson's platforms as well. We think availability of such tests will likely accelerate turnaround times, which is vital to the patient as well as for contact-tracing efforts and containment of new outbreaks.

Test, Mortality Data



Source: Cowen research report, July 24, 2020.

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For more information on COVID-19, please refer to the Center for Disease Control and Prevention at cdc.gov.

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