

COVID-19 Update 6

43 WEEKS AND COUNTING

October 15, 2020

COVID-19 by the Numbers: Cases, Deaths and Updated Guidelines

Confirmed Cases ¹ –Top Ten States and Nationally

State	Total Tested	As % of Pop.	Active Confirmed Cases	WoW % Change	% Actively Hospitalized
CA	16,333,717	41.3%	852,406	2.9%	0.4%
TX	7,012,023	24.2%	800,415	3.5%	0.4%
FL	5,593,424	26.0%	716,559	2.3%	0.3%
NY	12,230,436	62.9%	476,708	2.1%	0.1%
GA	3,180,548	29.9%	333,304	2.7%	0.5%
IL	6,414,292	50.6%	324,743	6.5%	0.5%
NC	3,444,583	32.8%	227,496	5.6%	0.3%
AZ	1,581,151	21.7%	221,804	2.1%	0.5%
NJ	3,972,585	44.7%	215,085	2.7%	0.3%
TN	3,225,624	47.2%	208,606	6.1%	0.5%
U.S. Total	117,420,096	35.8%	7,819,597	4.1%	0.5%

Greatest WoW % Change by State

State	WoW % Change
MT	27.8%
WY	17.2%
ND	15.9%
AK	15.1%
WI	14.0%
UT	10.5%
NE	9.5%
WV	9.0%
NM	8.9%
KY	8.9%
U.S. Total	4.1%

Recent Observations

- It has been 43 weeks since the first COVID-19 positive patient was tested in the United States, with a total death toll in the U.S. of ~216,000; just under 1M individuals are tested daily in the U.S., a ~2x increase since July
- The U.S. is averaging over 50,000 new confirmed cases daily, the highest numbers since mid-August; while hospitalization rates trend upward, the daily death rate has dropped to ~700 deaths per day, ~30% lower than the average in August
- As of today, 100% of states are reopened and are progressing through their respective plans; however, cases by state have been growing steadily, with over 44 states reporting rising infection rates and ~13 states reporting record numbers of positive cases**
 - While more populous states like California, Texas and Florida continue to display the highest amount of active cases, outbreaks across the Midwest have sent the national curve back on an upward trajectory
 - Although only representing ~28,000 total cases in the U.S., North Dakota is the state with the highest rate of cases-per-capita (~73:100,000), followed by South Dakota (~70:100,000), Montana (~52:100,000), Wisconsin (~46:100,000) and Utah (~37:100,000)
 - Infection clusters have accounted for ~70% of all hospitalizations in larger states such as New York and California
 - State plans in regards to the rollout of vaccines are due for submission by October 16, however many states are behind due to uncertainty surrounding the federal government's guidance on vaccine timing and expected involvement of the Department of Defense
- Globally, there have been over 37M total cases, driven by a second wave of infections in Europe as well as climbing rates in Brazil and India; the World Bank estimates that the COVID-19 pandemic is likely to push ~100M people into extreme poverty in 2020**
 - Experts state that the spike in European cases may be attributable to increased vacationing, travel and the reopening of schools; Spain has declared a State of Emergency while Italy and Germany have enacted considerable restrictions such as the closure of business, postponement of sporting events, and regional quarantines; major cities like London and Paris have reinforced lockdown procedures
 - Sweden, whose officials enacted policies promoting herd immunity by limiting lockdown procedures during the pandemic, has uniformly failed to limit mortality rates and continues to have the highest per capita rate of infection in Europe; this indicates that the herd immunity model of infection limitation may not be a successful roadmap
- Our understanding of the disease has continued to improve with increased observation and research**
 - According to a UCLA study, the average duration of antibodies for patients with mild infections is ~2-3 months, followed by a dramatic drop off in antibody levels
 - In October, the CDC reported that most infections are spread through close contact (<6 feet apart), not airborne transmission, with 40-45% of infections occurring without symptoms; airborne transmission has occurred under special circumstances due to prolonged exposure in enclosed spaces and inadequate ventilation or air handling
- In October, the first U.S. case of re-infection by two genetically-differentiated strains of the virus was confirmed**
 - The individual was infected twice over the span of two months, testing positive for differentiated strains in March and June; researchers have indicated that previous exposure to the virus does not guarantee total immunity; however due to the limited amount of recorded reinfections (~22 worldwide), the expected frequency of reinfection and the bodies immunological memory when battling the virus remains inconclusive
 - Some experts are anticipating moderate reinfection rates based primarily off of a 2018 study of a similar coronavirus (NL63) that became wide spread in Kenya; reinfection for NL63 was as high as 21%
- The new U.S. COVID-19 stimulus bill remains at an impasse**
 - On October 9, the White House increased its stimulus offer to \$1.8T, ~\$400B less than the \$2.2T bill House Democrats had previously passed
 - While deliberations are ongoing, Senate Majority Leader Mitch McConnell announced on October 13 that the Senate is preparing for an October 19 vote for a "targeted relief" bill, that would provide ~\$500B to support unemployment benefits, schools, hospitals and Paycheck Protection Program (PPP)
 - On October 15, President Trump publicly reversed his office's previous stance, stating that he would like to push for a stimulus package "[bigger] than either Democrats or Republicans are offering"; the White House has agreed to the Democrat's \$75B allocation for testing / contact tracing and has indicated that they would be willing to use the unspent \$300B from the initial CARES Act to provide immediate relief, including stimulus payments, PPP loans and airline / job support
 - Both parties have expressed support for additional stimulus payments, increased testing funding, an extension of the PPP and a revamped airline assistance package; President Trump has repeatedly stated that he would sign a bill authorizing another stimulus check immediately if no support is passed prior to Election Day
- Current projections from the Institute for Health Metrics and Evaluation indicate that the death toll will reach ~400,000 by February 2021**
 - Recovery and a return to normalcy continues to depend on: (1) access to reliable testing / monitoring solutions, (2) individual compliance with recommended behaviors and (3) availability of a vaccine
 - On September 16, the Director of the CDC, Dr. Robert Redfield, indicated to lawmakers that it would take about "6 to 9 months" to get the entire American public vaccinated, with a resumption to "regular life" expected by Q3 2021

What are the Treatment Options?

Treatments for the Critically Ill and Hospitalized

With the recent spike in COVID-19 cases across the United States and President Trump's positive coronavirus results, a heightened emphasis has been placed on the current therapeutics for the severely ill. Currently, a number of therapeutics are available for patients experiencing the most severe symptoms and those requiring supplemented oxygen, however, there are no approved therapeutics that have material efficacy across the spectrum of severity.

Current Standard of Care

Remdesivir (Veklury)

- Produced by Gilead, Remdesivir is an intravenous (IV) investigational drug that binds to the viral RNA, inhibiting viral replication
- A clinical study involving 1,063 COVID-19 positive patients showed a significant reduction of the median hospitalization times from ~15 days to ~11 days for those who exhibited severe symptoms
- Treatment costs range from \$2,340 and \$3,120 for those covered by public programs and private insurance labels respectively

Dexamethasone

- Dexamethasone is a low-dose steroid treatment that reduces inflammation and calms down overactive immune systems
- According to a study of 6,425 patients, dexamethasone reduced death rates from ~41% to ~29% for patients that required mechanical ventilation and from ~26% to ~23% for those requiring supplemental oxygen but not ventilation
- The steroid has been available for decades with wide distribution and has a relatively low cost ranging from \$6 - \$40

President Trump's COVID-19 Therapeutic Regimen

- On October 1, it was announced that President Trump had tested positive for the COVID-19 virus and was subsequently sent to the Walter Reed National Medical Center for treatment and monitoring
- Upon the onset of symptoms, President Trump was treated with Remdesivir (Veklury) from Gilead Sciences
 - On October 1, the FDA amended the EUA allowing for hospitals to access the drug directly from the manufacturer and authorized distributors, as production began to outpace demand
- The President received a single 8-gram dose of Regeneron's polyclonal antibody "cocktail", currently in clinical trials
 - Regeneron filed for U.S. FDA EUA on October 7; the Company currently has ~50,000 doses available
 - The therapeutic would only be available to patients with severe cases of COVID-19
- He was also prescribed the steroid Dexamethasone and provided with supplementary oxygen to manage respiratory inflammation
 - President Trump's blood oxygen levels dipped below 94%, fitting the National Institute of Health's criteria for "severe illness"
- In addition, the President was reported to be taking supplements such as zinc, vitamin D, famotidine, melatonin and a daily aspirin

New Treatments: Updates on Pipeline Therapeutics

Novel Multi-Antibody Cocktail (IV) **REGENERON**

- Dual-antibody cocktail targeting the SARS-CoV-2 spike protein (glycoprotein required for infection); filed for EUA last week
- Regeneron has isolated hundreds of virus-neutralizing antibodies and selected the top two antibodies based on potency and binding affinity
 - approach has been validated with successful treatment of Ebola Virus
- Phase III prevention trial being conducted on over 2,000 patients across ~100 sites in the US
- The Regeneron therapeutic is currently only available in experimental trials and the Company anticipates ~300,000 doses to become available over the next few months
- Early estimates suggest the antibody could cost between \$1,500 - \$6,500 per treatment

Other Antibody Therapeutics (IV)

Lilly

- On May 29, Eli Lilly, working with AbCellera, launched its first Phase I study for LY-CoV555, testing safety and tolerability in hospitalized COVID-19 patients; the study involved 452 patients with mild to moderate symptoms who had tested positive for COVID-19 within 3 days and had not been hospitalized
- 5 of 302 patients who received the drug ended up hospitalized (1.7%), a 72% reduction in risk relative to the placebo patients; a middle dose of the antibody reached the trial's primary goal of a significant reduction in the load of SARS-CoV-2 in the blood of patients after 11 days
- Additional trial for LY-CoV016 is ongoing, which binds to a different spike protein

Mesenchymal Stem Cells (IV)

sorrento
THERAPEUTICS

- Hypothesized to reduce acute lung injury through cell regeneration; mesenchymal stem cells lack receptors that viruses use to enter cells, providing resistance to infection
- Undergoing Phase I studies for the treatment of acute respiratory distress syndrome associated with COVID-19
- Sorrento Therapeutics, partnered with Personalized Stem Cells, is currently recruiting hospitalized patients for their first study (n~20)

Convalescent Plasma Therapy (IV)

- Utilizes plasma from recovered patients which is transfused into infected patients and has shown clinical improvement in a small study of 5 critically ill patients
- On September 22, the National Institute of Health expanded clinical trials of the therapy backed by \$48 million in funding from Operation Warp Speed
- Received emergency use authorization on August 23, however the FDA is not currently supplying plasma

Olumiant (Oral)

Lilly

- Eli Lilly's rheumatoid arthritis medicine is close to becoming the third therapeutic to receive U.S. FDA EUA; filed last week
- Paired with Remdesivir, patients time to recovery was cut by 12.5%, with a 35% cut in patients' death rate at the 29-day mark, in a recent study from the NIAID

Vaccine Update

Pre-clinical
170+ vaccines



Phase I
10 vaccines



Phase II
15 vaccines



Phase III
10 vaccines



Approved
0 vaccines

Company	Candidate	Type	Funding Raised (\$ in millions)	Phase	Status	Expected U.S. Approval
	BNT162	mRNA	\$1,950	Phase II/III	Recruiting	Nov. 2020
	AZD7442	Monoclonal Antibody	\$1,200	Phase III	Recruiting	Dec. 2020
	mRNA-1273	mRNA	\$2,500	Phase III	Recruiting	Jan. 2021
	NVX-CoV2373	Protein Subunit	\$2,058	Phase III	Recruiting	Jan. 2021
	Ad26 SARS-CoV-2	Non-Replicating Viral Vector	\$1,456	Phase III	Paused	Early 2021
	--	Adjuvanted Recombinant	\$2,000	Phase I/II	Recruiting	Mid-2021

Key Updates on Leading Candidates

- Given the severity of the pandemic, the first approved vaccine is expected to be released under Emergency Use Authorization and in the longer term may prove to not be the most effective
 - Additional approvals of competing candidates are likely to validate effectiveness over time
- BioNTech / Pfizer:**
 - October 6:** Initiated a rolling submission to the European Medicines Agency (EMA) for BNT162b2 following the release of promising pre-clinical and early clinical results; to date, the trial has enrolled over 37,000 participants with more than 28,000 having received their second vaccination
 - Topline phase I data showed 3.6x the geometric mean titers in younger adults, and 1.6x in older adults
 - Contracted with the U.S. government to supply 100M doses for \$1.95B, with option to acquire up to 500M additional doses; BioNTech expects the initial 100M doses to be ready by the end of 2020 with ~1.3B available in 2021
 - The vaccine is being tested at a 30 µg dose level in a two-dose regimen
- AstraZeneca:**
 - October 2:** Resumed phase I/II clinical trials for AZD1222 after a temporary pause on September 6 following one participant's adverse response to the vaccine (a form of inflammation known as transverse myelitis)
 - In phase I/II topline data, a single dose resulted in a 4x increase in antibodies in 95% of participants after one month (n=1,077)
- Moderna:**
 - October 14:** Received confirmation of eligibility for submission of a Marketing Authorization Application to the EMA
 - October 6:** Announced slow-down to Phase III trials due to insufficient demographic diversity
 - Currently expected to deliver its vaccine candidate in early 2021 with Canada receiving up to 56M doses
- Novavax:**
 - September 24:** Announced initiation of its first phase III study to evaluate the efficacy, safety and immunogenicity of NVX-CoV2373 and plans to enroll up to 10,000 participants
 - September 12:** Announced a manufacturing agreement with Serum Institute of India, increasing global production capacity to over 2 billion doses annually by mid-2021
- Johnson & Johnson (Janssen):**
 - October 12:** Phase III trial paused as the Company investigates a study participant's "unexplained illness"
 - October 8:** Announced European Commission Approval for JNJ to supply EU members states with 200M doses with the option to secure an additional 200M pending approval / authorization from regulators. The Company currently expects the vaccine to become available in early 2021 under an emergency use authorization
 - JNJ's vaccine candidate does not require freezing and is potentially a one dose regimen, compared to two for competitor
- Currently, there are 5 vaccines globally that are approved for limited use produced by: Sinovac (China) Sinopharm (China / U.A.E), CanSinoBio (China) and the Gamaleya Research Institute (Russia)**
 - These candidates have been given emergency approval for use on health care workers and military soldiers as Phase III testing continues; to date, there are no comprehensive reports on updated safety and efficacy of these vaccines in limited use

Phase 1:
Approval in Nov.;
First responders and medical
workers within first 4 weeks

Phase 2:
Group homes, older
adults/underlying health
issues in first 2 months

Phase 3:
Service industry workers
and young adults in early
2021

Phase 4:
Remaining individuals or
lottery system by Q3 2021

U.S. Sentiment on Vaccines

- As of October 10, ~48% of U.S. adults say they would choose to receive a COVID-19 vaccine if it were available today, as opposed to 72% in April
 - Ongoing polling has shown that the decrease in willingness was fueled by a sharp drop in mid-August, around the time reports of White House interference at the FDA and other federal health agencies began to command more public attention
 - As of September, ~77% of Americans believed that it is likely a vaccine will be approved before safety and efficacy are fully understood
 - However, willingness to get vaccinated has crept up 2% since early September, following the presidential and vice-presidential debates

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