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COVID Drug Pipeline Updates

Reasonable hope while keeping expectations grounded
What we expect to see over the next 18 months

Every day our country is inundated with a dynamic and ever-changing stream of information regarding the latest virologic contagion to sweep the world: COVID-19. On TV, through email and social media news feeds, most of the stories are the here-and-now or lessons from the recent past.

But what will the future hold?

Here we present a high-level overview of the COVID-19 related drug pipeline and a look into how researchers around the globe are racing to find treatments to defeat this viral enemy.

TOPICS COVERED IN THIS UPDATE

WITHIN WEEKS
Older, traditional drugs being re-purposed

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WITHIN MONTHS
Specialty drug clinical trials will emerge

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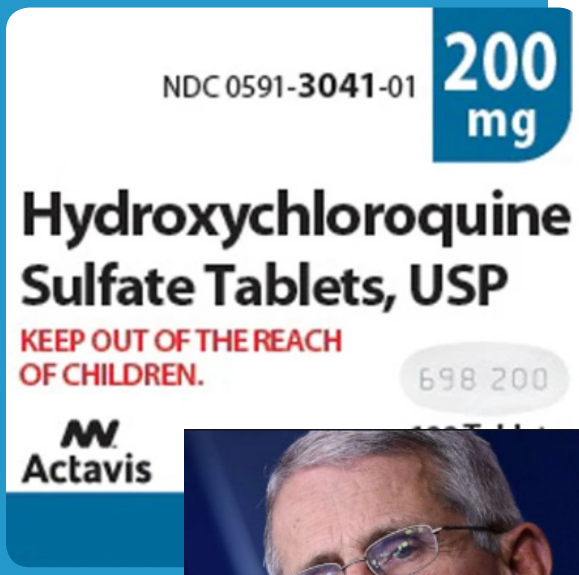
IN ABOUT A YEAR
Development of vaccines

WITHIN WEEKS
Data emerges on older, traditional re-purposed generic drugs

There are currently no FDA-approved therapies to treat or prevent COVID-19. To date, there are case reports of small-scale studies of commercially available agents used off-label in patients. Anti-malaria drug products such as chloroquine and hydroxychloroquine as well as antibiotics such as azithromycin have emerged as early treatment options with less-than-definitive positive outcomes. HIV antivirals, lopinavir and ritonavir (sold as Kaletra® or Aluvia by **AbbVie**), gained some hype although short-lived, ultimately showing little to no benefit. Again, none of these therapies are approved specifically for COVID-19.

Physician and coronavirus task force committee member **Dr. Anthony Fauci** stated in a White House press briefing on March 20, **"We're trying to strike a balance between making something with a potential of an effect to the American people available, at the same time that we do it under the auspices of a protocol that would give us information to determine if it's truly safe and truly effective."**



Given the attention some of these products have received in the media, we have seen a spike in utilization on the pharmacy benefit, despite clinical data not yet showing clear efficacy. Within the next few weeks, drugs like **hydroxychloroquine and azithromycin** will be tested in a large, controlled, randomized environment to allow robust data collection and evaluation of the benefit versus risk in patients infected with COVID-19. In the meantime, the FDA has granted emergency use authorization (EUA) for chloroquine and hydroxychloroquine, allowing licensed practitioners to obtain product supplied from the Strategic National Stockpile (SNS) to treat patients "for whom a clinical trial is not available or participation is not feasible".

Convalescent Plasma: Aside from drugs, can someone else's antibodies treat my COVID-19?

We will soon find out. Several institutions are studying the use of blood plasma collected from patients who have completely recovered from a COVID-19 infection. The plasma is free of virologic pathogens, but contains immunoglobulins believed to help boost an immune response and lower mortality risk. **FDA Commissioner Stephen Hahn said the agency is "really pushing hard to try to accelerate" the use of convalescent plasma in severe or immediately life-threatening COVID-19 patients**.

As the FDA works to determine safety and efficacy of using blood plasma, a licensed physician must request approval for access on a case-by-case basis submitted through an expedited regulatory pathway referred to as emergency Investigational New Drug Applications (eINDs).

WITHIN MONTHS
Specialty drug clinical trial results will emerge

We are tracking an ever-growing list of 115 molecules in pre-clinical and clinical development within the US for COVID-19, representing research efforts across almost 100 pharmaceutical companies. These products span many different molecule types including small molecules, proteins, monoclonal and polyclonal antibodies, cell therapies, and vaccines among others. Of note and furthest along in clinical development within the US are specialty medications sarilumab by **Sanofi**, tocilizumab by **Roche**, and remdesivir by **Gilead Sciences, Inc**.

Monoclonal Antibodies: Drugs that work to reduce inflammatory pathways in the body

Sarilumab and tocilizumab do not directly target the coronavirus; they are classified as monoclonal antibodies and believed to inhibit a key signaling pathway that drives the inflammatory immune response causing acute respiratory distress syndrome, and possibly death, in critically ill COVID-19 patients. Interestingly, both are commercially available in the US and approved to treat Rheumatoid Arthritis.

Sarilumab is marketed under the trade name Kevzara®, and tocilizumab is marketed under the trade name Actemra®.

According to recent press releases, controlled clinical trials will evaluate the safety and efficacy of adding sarilumab or tocilizumab to usual supportive care compared to supportive care plus placebo in patients hospitalized with severe COVID-19. Drug sponsors will assess the impact on fever duration and patients' need for supplemental oxygen as well as outcomes including mortality and reducing the need for mechanical ventilation, supplemental oxygen, and/or hospitalization.

Based on positive preliminary results, China's National Health Commission (NHC) recently updated its COVID-19 treatment guidelines and approved the use of sarilumab and tocilizumab to treat patients with severe or critical disease. Unlike many of the re-purposed generics being studied, we expect these specialty products will only be used in inpatient settings.

Direct-acting Antivirals: Drugs that block the virus from multiplying

Infectious disease powerhouse **Gilead**, well known for its Hepatitis C treatments, is also aiming to provide an anti-viral option for COVID-19 patients with its investigational new molecular entity remdesivir.

Unlike sarilumab and tocilizumab, remdesivir is not yet licensed or approved in the US and has not been demonstrated to be safe or effective for any indication. But for the past decade, it has been tested as a general antiviral candidate and as a lead candidate against the Ebola virus. **Gilead** will conduct two studies in approximately 1,000 patients to evaluate both a 5-day and a 10-day dosing duration of remdesivir administered intravenously in patients with moderate or severe manifestations of COVID-19. The primary objective is to measure the normalization of fever and oxygen saturation as compared to standard of care alone. Remdesivir is believed to work by blocking the virus' cellular replication messaging process, thereby preventing the virus from multiplying.

Trial results are expected within the next month. Until then, reports of the drug being used in compassionate use and expanded access situations gives hope during a time of global crisis.

Another antiviral of note, favipravir, in development outside the US has also garnered publicity based on potential success in small case studies. Experts are less optimistic with the therapeutic viability of favipravir as adverse effects and safety concerns may outweigh the drug's benefit. Results from a larger trial in China are expected in June.

IN ABOUT A YEAR
Vaccines become available

Of the 115 molecules we are tracking in development within the US, 39 are categorized as vaccines. Many big pharma companies including **GlaxoSmithKline**, **Eli Lilly**, **Pfizer**, **Sanofi**, and **Johnson & Johnson** have already announced plans for vaccine trials. Smaller biotechs, such as **Inovio Pharmaceuticals**, **BioNTech**, **CureVac**, **Moderna**, and **Arcturus Therapeutics**, are also making progress, some with unique manufacturing approaches that may allow an accelerated development timeline. Researchers are banking on about 8 different techniques to prime the body to fight infection. Some are focused on using viral DNA to generate antibodies without causing infection, and some are using RNA technologies to encode the production of protective proteins.

"The reality is we can get a therapeutic, I believe, by the fall… this is achievable."

Dr. Scott Gottlieb, former FDA commissioner

In summary, a variety of approaches are being taken, but they all share the same goal—to create a product that allows the body to produce antibodies that naturally protect against the virus.

With most vaccines in pre-clinical development, human studies to determine safety are set to begin within the next few months. One manufacturer, **Inovio**, believes its vaccine candidate will progress through clinical trials and be available by the end of this year. **Moderna** is also confident their vaccine, which is currently in Phase I clinical trials and has now been dosed in humans, can be available to healthcare workers in the fall of 2020… just a few months away! **Johnson & Johnson** hopes to begin testing in humans by September of this year with a launch goal of early 2021. This relatively short turn-around time would not be possible without the promised support from The Department of Health and Human Services, specifically the Biomedical Advanced Research and Development Authority, or **BARDA**, division. Together with **BARDA**, **Johnson & Johnson** announced publicly they will contribute $1 billion towards COVID-19 vaccine efforts.

As the world remains largely in social isolation, researchers and health care leaders are collaborating to combat the devastating effects of COVID-19 and find a solution. Dr. Scott Gottlieb, former FDA commissioner, is optimistic stating in an interview with CNBC on March 17, "The reality is we can get a therapeutic, I believe, by the fall… this is achievable."

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