Coronavirus: The Signals to Watch

How the virus is changing health care investing.

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KEY INSIGHTS

- The new coronavirus is proving more infectious but less deadly than originally estimated.
- Several treatments under development appear to hold promise and should provide a bridge to an eventual vaccine.
- We are tracking the pandemic's imprint on the sector, but we continue to invest in a range of therapies and services that should improve outcomes and reduce costs.

In attempting to anticipate the course of the coronavirus pandemic and its impact on the health care sector, we are leveraging our team's medical and scientific backgrounds as we gather information and seek insights. Our combined experience is proving valuable as we consult with disease experts, including epidemiologists, virologists, former Food and Drug Administration officials, and doctors on the front lines treating patients. Frequent discussions with company managements also remain a key part of our investment process. We are in close contact with firms pursuing vaccines and treatments, as well as those focused on testing and other supplies related to the virus.

What We Are Learning About the Virus

Because the virus has been in humans for only five months, the scientific community's understanding of the key variables—including the virus's infectivity and lethality, as well as the nature of the human immune response—is still evolving. In our analysis of the research, we have iteratively tried to determine the most likely scenarios for the course of the pandemic as our understanding of the virus improves over time. Thankfully, we have been able to discard the worst-case outcomes, but we also think it is highly unlikely that the world can soon return to normal.

Our general conclusion is that the new coronavirus is steadily appearing more infectious but less deadly than suggested by early evidence from China. The most important variable in epidemiology models is the rate of transmission, as represented by R0, or the average number of other individuals a single infected person is likely to infect. The difference between an R0 of two or six may be the difference between a few thousand or a few million infections over a short period. For reference, the flu's R0 is between one and two; at the other

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end of the spectrum, the R0 for measles ranges between 12 and 18.

To date, we estimate that the R0 for COVID-19, the disease caused by the coronavirus, is somewhere above three but well below 10. Several factors make the disease highly infectious: the long incubation period, the large proportion of asymptomatic patients, and the virus's ability to survive for long periods on surfaces and even in the air.

The Fatality Rate Is Likely at or Below 1%

The accumulating evidence on the virus's fatality rate is more encouraging. Early reports from China suggested that the fatality rate was as high as 3%, but it is clear now that this figure reflected a skewed denominator because of the lack of testing. Indeed, in those rare settings where over 10% of the population has been tested, the fatality rate has proved to be as low as 0.5% or less.

The most important implication is that the number of infected people is far higher than the number of reported cases, and as the number of fatalities continues to rise, so does the likely percentage of the population that has been infected. Nevertheless, the number of current fatalities suggests that only a small part of the population now has immunity as a result of past infection—meaning that we are still far from achieving herd immunity. Based on experience with past epidemics, at least 60% of a population needs to be infected to stop the virus without a vaccine or other interventions. Assuming a 0.5% fatality rate, this would imply about 1 million fatalities in the U.S. (330 million x 0.6 x 0.005) if steps such as social distancing were not taken and no treatments developed.

The Evolution of the Pandemic in the Coming Months

The virus seems to have caused fewer deaths in warmer countries, which fits the pattern of respiratory viruses usually spreading the most in cold, dry conditions. We are optimistic that the number of new infections in the U.S. will fall off considerably by late summer. The extent to which the virus will then return in the fall will depend on the effectiveness and duration of the current lockdown, the availability of testing, and the new treatments then widely available. Better testing and mitigation efforts are likely to limit regional outbreaks, as has happened in Hong Kong and Singapore. While previously exposed individuals could be reinfected, experience with other viruses suggests the severity of the illness should be much lower.

Behavioral changes, particularly the widespread wearing of masks, will also be key in limiting further waves of infections. Governments initially claimed they were ineffective to prevent hoarding by the public and to reserve them for health care workers. Yet it is clear that common masks, if not as effective as N95 respirators, do provide some level of protection. Policymakers will have to pivot away from their no-mask message while preserving the public's trust, which will be a delicate exercise.

The Availability of Effective Treatments

The development of effective treatments for COVID-19 patients will be crucial over the coming months, both in preventing fatalities and in assuring people that it is safe to begin resuming normal life. Fortunately, many biopharmaceutical companies are focused on developing treatments, and several are promising.

Much recent attention has focused on Gilead Sciences' remdesivir, one of a class of direct-acting antivirals (DAAs) designed to block the replication of the virus. We have seen some good efficacy for DAAs in treating related viruses, such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). DAAs may pressure the virus to mutate, however, and these drugs typically work best in the earliest stages of the disease, when the impact of inhibiting the replication of the virus is greatest. Roche's blockbuster flu drug Tamiflu, for example,

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can only be used during the first 48 hours of infection with flu.

Another area of treatment is the use of antibodies to help fight off the disease. These can be harvested from the plasma of those who have recovered from the virus, but this relies on a favorable ratio of donors to patients. To get around this hurdle, companies are working on scalable approaches using mice engineered to mimic the human immune response. Even in this case, the resulting number of antibody treatments would probably number only in the millions, meaning that they would likely be used for prophylactic purposes for health care workers or other high-risk groups.

Finally, existing drugs from Roche and Regeneron may dampen the immune cascade in the late stages of the disease—the so-called cytokine-release syndrome, which can prove fatal in some cases. Interleukin-6 inhibitors developed by the two companies to treat inflammatory diseases and cancers seem to present a reasonable chance of reducing the severity of the body's immune reaction to the coronavirus.

Prospects for a Vaccine

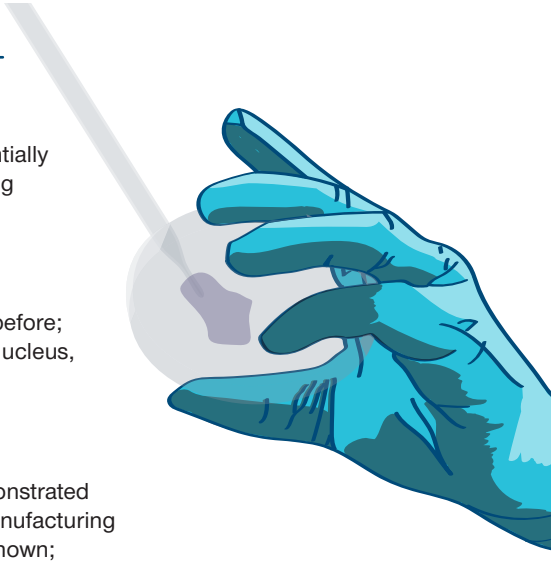
The hope is that we will deploy these treatments as a bridge to get us to the ultimate endpoint of the crisis—the development of an effective vaccine. Thankfully, a successful vaccine appears likely given that we are aiming at a relatively stable target. To date, we have been confronting a single strain of the virus, and coronaviruses do not tend to mutate significantly.[1]

A vaccine that targets a spike protein on the coronavirus—one using a traditional "subunit" approach—appears most likely. The weakness of subunit vaccines is that immunity may not be as robust as with certain other technologies, but the technology is well characterized with several successful commercialized vaccines, including those for hepatitis B,

The Race for a Vaccine Is in Early Stages

Those in development fall into three categories.

Categories	In Theory	In Practice
Subunit Vaccines 	Primarily targets the virus's spike protein so the immune system can respond to a piece of the virus not needed for replication	Safe and well established, but may lead to suboptimal or temporary immunity, thus potentially requiring substantial engineering
DNA Vaccines 	Contains DNA that codes for specific proteins of the required pathogens	Relatively new technology; only approved for human use once before; difficult for DNA to enter cells' nucleus, thus requiring engineering
mRNA Vaccines 	Introduces an mRNA sequence (which provides instructions to cells on what to make) coded for a specific disease antigen	Early research has not yet demonstrated protection against infection; manufacturing at large scale has never been shown; RNA is fragile—must be encapsulated in lipid



Source: T. Rowe Price.

[1] As noted previously, as information regarding the virus is still evolving, this is subject to change as more research is performed.

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human papillomavirus, and the seasonal flu. Given the breadth of efforts being undertaken in the field, more than one vaccine is likely to be deployed given the scale of the population that needs to be quickly inoculated.

The need to avoid cutting corners on safety on a vaccine—given that billions of doses will need to be procured—means that it might take more than the 12–18 months that has been widely floated in the press to have one widely available. Trials must be large enough to be able to detect rare but potentially disastrous side effects across a wide range of demographics, such as children, pregnant women, and the elderly.

Investment Opportunities and Challenges as Companies Respond to COVID-19

Many biotechnology and pharmaceutical firms developing treatments or a vaccine for COVID-19 have attracted keen investor interest and appear to be valued based on hope rather than on realistic chances of clinical or commercial success. Initially, as the market collapsed, we took advantage of dislocations and inefficiencies created by liquidations and panic selling. Our process is unchanged: We continue to invest in what we believe are well-managed companies with disruptive new product candidates and those with proven, productive research and development platforms.

Indeed, the longer-term impact of the crisis is likely to cause investors to put an even greater premium on innovation and novel drug platforms. This should result in an even wider spread in valuations between "high value" and "low value" medicines. With biopharma innovation accelerating—and this being one of the few areas that has been resilient through the pandemic—we expect there will also continue to be meaningful new investment opportunities in the form of initial public offerings.

A New Perspective on the Trade-Off Between Drug Pricing and Innovation?

Relatedly, the intense focus on the importance of drug development during this crisis is likely to change public perceptions on the trade-off between drug pricing and innovation. As the regulatory overhang diminishes, valuations in the sector are likely to benefit. Likewise, diminished political risk in the form of a drastic overhaul of the U.S. health insurance system may provide a tailwind for managed care firms, at least in the intermediate term.

We are keeping an eye on other changes that are likely to prove more specific to companies and industries. More health care will be conducted virtually now that telehealth has demonstrated its viability and cost-savings. Likewise, patients are likely to turn to drugs delivered subcutaneously at home rather than intravenously at a medical facility. In addition, people are turning to pets for comfort and companionship, and companies focused on animal health stand to benefit.

Generally, we continue to invest in treatments for a wide range of conditions that seek to improve the standard of care and meet unmet medical needs, as well as services that improve access to and affordability of health care. We are confident our emphasis on taking a longer-term view and identifying investment ideas through fundamental, bottom-up research should continue to add value for our clients.

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