



INVESTMENT INSIGHTS

A Conversation About Coronavirus



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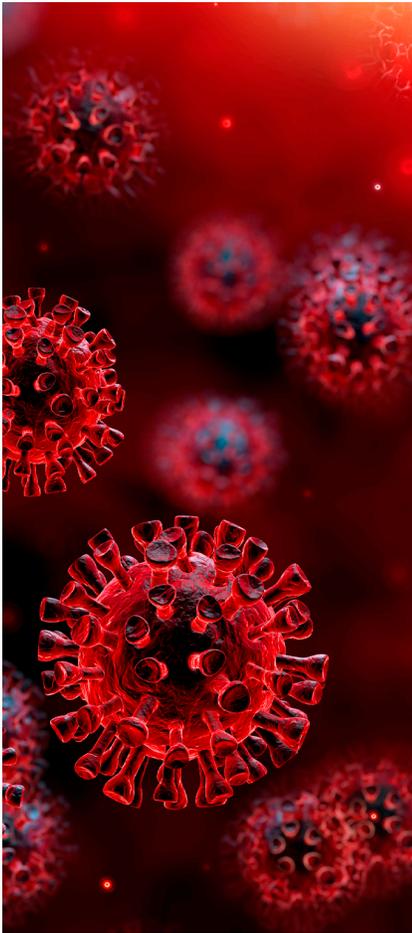
On February 28, markets plunged, wiping out 2020's gains, in the wake of fears around the spreading coronavirus to outside Asia, including the U.S. In an effort to better understand the science behind the epidemic that was driving down markets, Chief investment Officer Tony Roth sat down with Dr. Amesh Adalja. A Fellow with the Infectious Disease Society of America, Dr. Adalja is also a Senior Scholar at John Hopkins' Center for Health Security. He practices medicine and focuses on emerging infectious diseases, pandemic preparedness, and biosecurity. He appears regularly on major media outlets as an expert on coronavirus. Here are excerpts of their conversation (edited for length and clarity), with critical questions asked and answered...

TR: In nearly 40 countries, there are roughly 85,000 reported cases and nearly 3,000 deaths due to coronavirus. And in the U.S., we recently had the first diagnosed case of a community transmitted case, meaning it was not able to be traced to someone who caught it from someone who had been in China or another source. What is your view of its transmissibility and how does it compare with prior epidemics like SARS and MERS?

AA: Coronavirus has an incubation period that can last up to 14 days, six days on average—and there may be some evidence that toward the end of that incubation period just before you get symptoms, you may be contagious. That's what makes it harder to control but what's driving the spread is its human-to-human transmission. You get more virus particles in your nose and throat than with SARS, for example, and that makes you much more contagious than SARS and MERS which didn't have that ability to transmit efficiently from human to human. That's what allowed them to be contained but is allowing this virus to spread. And remember coronaviruses are part of a big family of viruses and some of them do cause the common cold. This one is behaving in its transmissibility more like the common cold type of coronaviruses vs. SARS or MERS.

TR: Let's turn to mortality rate. The numbers on that out of China are questionable relative to the number who have contracted the disease. There's also the suggestion that people there may be more susceptible due to poor air quality, more smokers, and potentially lower-quality health care. Do we have a sense yet as to what the mortality rate is? How does it compare to the flu?

* The opinions of Dr. Amesh Adalja are his own and do not necessarily represent those of Wilmington Trust, M&T Bank, or any of its affiliates.



AA: The case fatality ratio is one of the big mysteries. We know it has the capacity to cause severe illness and kill, but we don't know the ratio. How likely that is to happen has to do with the fact that we're not testing widely. We're not testing mild cases of those with just a runny nose or sore throat. We're testing patients that come to hospitals and health care facilities, so that introduces a severity bias into the data.

When you see a case fatality rate in Wuhan or in Hubei Province of 2% you have to interpret that with caution because it's skewed. In China outside of Hubei Province the case fatality rate drops to below 1% outside of Wuhan. So there may be co-factors going on in Wuhan including smoking and smog and all the other differences that we're trying to tease out, but we don't quite know. And I suspect when this is all said and done the case fatality rate is going to be less than 1% and probably maybe a little bit worse than seasonal flu, which is around .01%. But we don't quite know yet, and the only way we're going to answer that is by increased diagnostic testing.

TR: **Do you think China is getting ahead of the curve here and it's going to start to subside there, or do you think it's unlikely there will be a tapering off anytime soon? Or does the fact that factories are all starting back up there signal the possibility of a broader outbreak?**

AA: I don't think that we're going to see a tapering off in the short term. China has taken an aggressive approach to create major quarantine zones of over 40 million people, but I don't think we can credit the government with a decrease in transmission. It actually made things worse by creating shortages and problems with logistics there and panicking the population—prompting them to flee to other cities. It was actually an example of how to not handle the outbreak. Also, this is a respiratory virus that spreads efficiently and has a wide spectrum of illness. I don't think this is a containable type of virus. There is some seasonality to coronaviruses in temperate climates like the Northern and Southern Hemispheres that, as the season moves to warmer months, there may be some tapering off, but maybe not. It might go away when the Northern Hemisphere warms. That doesn't mean it's not in the Southern Hemisphere or the Tropics when it becomes warm, because the Southern Hemisphere has the opposite seasons and the Tropics don't really have seasons, so viruses there don't have that seasonality.

As far as restarting factories in China, that is hopefully an acknowledgment that this isn't a containable virus, so there's no need to disrupt everybody's lives with restrictions that aren't going to appreciably change the force of the outbreak. So opening factories is a good sign, but it's just a coping mechanism moving toward a new normal because the virus isn't going away. It's going to become endemic in human populations, which means it's going to be with us the way influenza is with us until we have a vaccine.

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TR: Is it inevitable that this is going to be a pandemic? How much time do we have?

AA: I don't think we have any time. If you look at this from an infectious disease position, we're in the midst of a pandemic. This virus started spreading in November and the first case was reported December 1—so if you have a respiratory virus that has efficient ability to transmit and you give it that much of a head start, it's everywhere. And what you're seeing in many countries is just the tip of the iceberg because, as I said earlier, most of these cases are mild and we are not testing the mild cases, so what is to say that there are not mild cases in other parts of the world that are mixed in with our cold and flu season? I think most people are going to be infected or at risk and it's going to be like the 2009 H1N1 influenza pandemic. Since this is a novel coronavirus, maybe up to 40% or half the population based on extrapolating numbers from other outbreaks of novel viruses may be susceptible.

TR: Is there a therapeutic treatment that may be helpful at this stage?

AA: There are no specific antivirals that are licensed for coronaviruses, but we do know that Remdesivir has activity against coronaviruses and it was given in an experimental basis to our first American patient in the state of Washington. And it has now been entered into a Phase 2 clinical trial where they're enrolling between a couple and several hundred patients to see if it has efficacy. We'll need to work out dosing, which patients benefit the most, the side effects, and the time window when it's most effective. There are other drugs in trials, too, but Remdesivir is the lead right now.



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TR: As far as a vaccine goes, given the seriousness of the global situation, is there any way governments can work to expedite the testing process around these vaccines that seem to be on a new track in terms of how quickly they're developed?

AA: That's the big question. We do use new technologies now, both with the Moderna and Inovio's candidates, and Moderna already delivered its vaccine to the NIH for a clinical trial. But clinical trials take time. You have to look for safety and have a big enough population to actually see safety signals that may occur only in like 0.01% of patients. You have to figure out the dose and the number of doses, and then measure and test antibodies in a test tube to see if they're actually blocking the virus. After that, you keep doing bigger and bigger trials. It's going to take time to get through those trials. It's going to be a very long process, even with the FDA's expedited review process called the Emergency Use Authorize, which we've seen used for other products that can allow things to be put onto the market before they're officially FDA approved. Then there's still the steps of manufacturing at a scale that's large enough to vaccinate the at-risk populations of the world. That's why we're saying at least 12 to 18 months before we have vaccines for the population.

TR: So is the end game here that one day we're all going to get a flu shot and coronavirus is either going to be a second shot or a series of shots, and we'll all get vaccinated?

AA: That would be the hope, to develop a coronavirus vaccine, maybe even a universal corona vaccine that's effective against all six human coronaviruses. That would be really game changing in terms of removing coronaviruses as a threat for pandemics. But the hope would be that it is part of childhood immunization.

TR: How prepared are we in the U.S.? Are there additional things that our government should be doing?

AA: The U.S. likely has the best preparedness of any country against infectious disease emergencies. We've been at this at least since 2001 with the anthrax attacks. So we are pretty good at that, but there are gaps and there are places where preparedness has eroded. Our health care system is overstressed and working at near capacity all the time, so that even a bad flu season can put a hospital into problems because they can't cope with the surge of patients. We also are woefully inadequate in diagnostic testing capacity, and we are unable to test large numbers of individuals. We have very strict testing criteria in the U.S. We need to have more kits. We need commercial apps to be making kits.

We also need to get faster at doing clinical trials and vaccine trials. We're going as fast as we can, but I think that could be improved. And we also have to get much better at public health communication because there's a sea of misinformation that's out there. I think that the trusted sources of information need to be able to rise above all of the cackling of the Russian bots and everybody else that's exploiting this outbreak and spreading rumors and misinformation and myths about this virus.

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TR: We've read that we shouldn't go out and buy masks, and that we should make sure we stock up at home on the medicines we take regularly, but is there anything else we should know or do?

AA: Learn about your own community and understand what the avenues are for infectious disease control, meaning do you have a local health department? Do you have a county health department? Who's going to be making those decisions for your community, where is that information going to come from, and how are you going to be able to give feedback and engage with that process? So I think it's good to have that knowledge beforehand, before these decisions start getting made so you can actually be apprised of them and actually offer input into them. The same is true at your workplace; understanding what the rules are for telecommuting and teleworking if you can't come into work or if your kids are sick and you have to take off work; making sure that those policies are at least known to you by that time or at least addressed. The same goes for your children and their schools, and understanding those policies as well in addition to the general preparation. So I would advise people to do that.



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