

# THE YEAR OF LIVING DANGEROUSLY



Hamish Douglass, the Chairman and CIO at Magellan, explains the intricacies around the vaccines for the virus behind the covid-19 illness, warns a mutant variant could appear and tells why that's just one risk that could catch out investors in 2021.

## Q1. Why do you think 2021 is the Year of Living Dangerously?

This is the most complex risk environment the world has seen for many years. To get a sense of what could go wrong, imagine recent times as a Netflix series.

**Season 1 would be titled The Pandemic.** The series would track the outbreak of the influenza pandemic that started in Wuhan in China. Season 1 made viewers edgy until the final episode when global euphoria broke out and stock markets roared after scientists defied expectations and found a powerful vaccine to defeat the virus.

**Season 2 is where we are now, The Year of Living Dangerously.** While the director has commenced filming Season 2, the ending is still being decided. The director has instructed two teams to write different scripts. One option is subtitled The Awakening and it's a celebration of the ability of the vaccines to end the virus. This series documents how society and economies recover from the pandemic but it too has two different endings. One is a relatively smooth ending with a rapid but controlled economic recovery. This would be a nirvana outcome for financial markets. But the alternative ending is not so happy. Excessive stimulus leads to a lasting outbreak of inflation that triggers the next worldwide downturn as central banks abruptly raise interest rates. This would be a nasty shock for financial markets. The alternative script for Season 2 is subtitled The Mutant Strain. This plot is a dark tale of how a variant of the virus emerges that evades the vaccines and sets the world and financial markets back.

The plots outlined are possibilities yet there is little risk priced into markets at the moment. That makes the next 12 months a dangerous time for investors.

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## Q2. Should we have confidence in the vaccines?

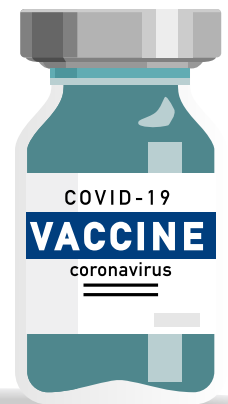
To evaluate the vaccine, we need to understand how the immune system fights infection. At a basic level, there are four integrated mechanisms in our immune defence system. T cells called CD4 are the intelligence service of the immune system because they recognise there is a virus in our bodies before our cells become infected. These cells then send out signals to fire up the immune system. That mobilises B-cells. Their job is to produce antibodies to stop the invading virus from entering our cells. Antibodies are the fighting forces that attack the invading virus simultaneously. Then there are T cells that are called CD8 or killer cells. These cells are our last line of defence if the antibodies fail to stop the viral invasion entering our cells. These killer cells can recognise that a cell has been infected by the virus. They try and kill these cells.

The vaccines are easy to grasp conceptually. Scientists have taken high-resolution pictures of the blueprint of a critical part of the virus and from these pictures they identified that the coronavirus has a large probe that locks onto cells in order to invade and infect cells. This probe is called the S or Spike protein. Scientists then worked out if they showed our immune system an exact copy of the blueprint of the Spike protein then it could trick CD4 T cells to remember what this looks like and they could work out what instructions to give to the B-cells. So the vaccines are effectively prewarning the immune system.

The shortcoming of this approach is that the immune system has only been shown the plans for the Spike and not the blueprint of the entire virus.

A good question to ask is why scientists didn't develop a vaccine with the entire blueprint. The answer is that this approach, while theoretically superior, is far more complex and it would take much longer to develop a whole-of-virus vaccine. The good news is that this approach is being worked on.

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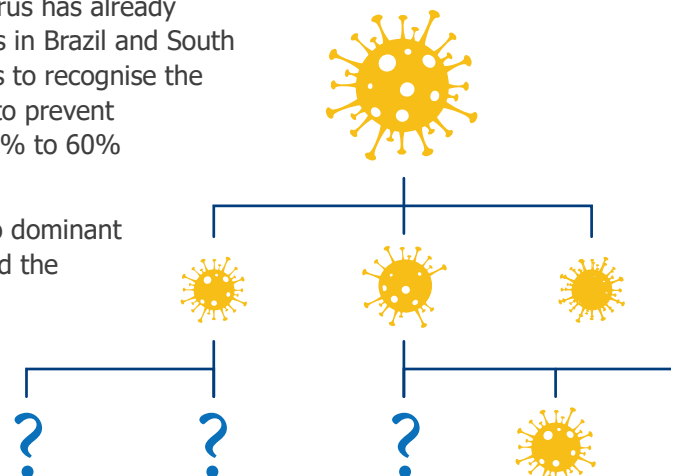
## Q3. How likely is a strain so mutant that it derails the assumed economic recovery?

The only way to assess this risk is to be guided by the science. Every time the virus replicates it needs to make a copy of its blueprint, which is known more formally as Ribonucleic acid or RNA. This replication happens perfectly millions and millions of times. But every now and then the replication is imperfect.

If the blueprint for the Spike protein probe changes, the CD4 T cells (intelligence service) become less able to recognise the Spike protein. As the Spike protein changes shape, the intelligence service may send fewer instructions to the B-cells, which means the immune system creates fewer antibodies. After enough mutations in the Spike protein, the immune system might be unable to recognise the Spike protein and an escape mutant emerges. An escape mutant is likely to quickly become the dominant strain of the virus.

The evidence shows that copying errors are occurring and the virus has already undergone significant change. Studies have found that mutations in Brazil and South Africa have significantly undermined the ability of the CD4 T cells to recognise the Spike protein and the B-cells are deploying far fewer antibodies to prevent infection. Results are finding the major vaccines are now only 10% to 60% effective in preventing symptomatic infection in South Africa.

Conversely, there is evidence that the UK mutation (which is also dominant in Israel) and the US mutations have not significantly undermined the ability of CD4 T cells to instruct B-cells to produce enough antibodies. That means vaccines in these countries remain highly effective. What is occurring in Brazil and South Africa is far more relevant in assessing the risk that the virus escapes.



## Q4. How easy would it be to recode the current vaccines for an escape mutation?

Unfortunately, the answer to this question appears to be: 'it depends'. There are two types of changes that may occur to the Spike protein as it mutates. The first type is an alteration in the shape of the Spike protein. This should be easy to recode for as you could take an exact copy and show the new blueprints to the immune system and it would be rearmed with the correct information.

The second type of change is what we would call a stealth change. This change makes part of the Spike protein effectively invisible to antibodies. This type of change may be much harder to recode vaccines for.

There is some evidence that shape and stealth mutations are occurring. We don't know the threat posed by these stealth mutations.

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## Q5. Some people say that, while the vaccines are becoming less effective in preventing infection in Brazil and South Africa, they remain effective in preventing deaths. Should we take comfort from this?

It's true that the vaccines are helping to prevent deaths in Brazil and South Africa. But we take little comfort from this observation as it is a snapshot in time, the virus will evolve and the vaccine efficacy is already compromised.

Studies have already concluded that future mutations could enable the virus to change in such a way as to evade the antibody response developed by the current vaccines. A lab experiment made public in December showed that, following the mutation known as E484K that is found in Brazil and South Africa, two other mutations occurred that enabled the virus to evade all antibodies present in the lab experiment. Concerningly, these mutations appeared to be of the stealth type. Whether or not these types of mutations occur outside labs is unknown. But they are foreseeable.



## Q6. It appears many investors are ignoring the risk of an escape mutant. Why are they overlooking this danger?

We think some powerful heuristic biases are at work that are blinding people to this risk. These biases include confirmation bias, the tendency to oversimplify, the 'fear of missing out' and the neglect of probability. The last term refers to how most people don't think in terms of risk and probability. Once they have determined a course of action, they either ignore other scenarios or dismiss the probability of these events occurring.

We are seeing some powerful examples of confirmation bias at play. In February, three studies were released on the same day. Two of them, one from Israel and the other from Scotland, were glowing while the other posed a warning. This was the study that showed the Astra Zeneca/Oxford vaccine in South Africa was only 10% effective in preventing mild to severe infection. The first two studies received positive and wide global media coverage that cheered investors. The bleak results from South Africa went largely unreported and were seemingly ignored by equity investors because on the same day travel-related stock rallied.

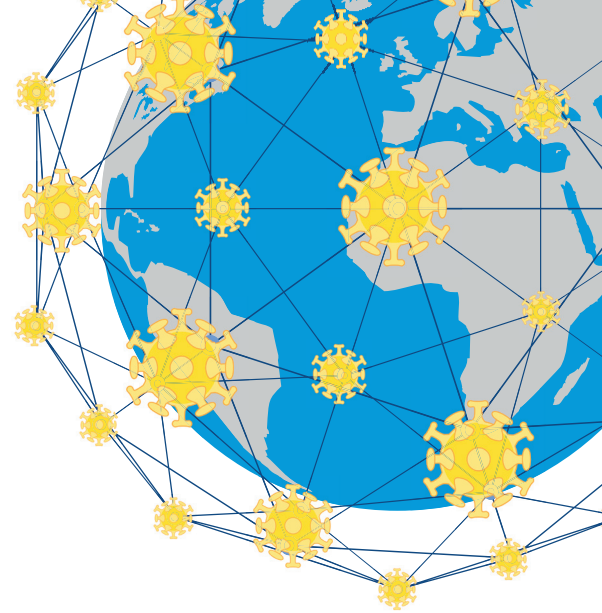
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## Q7. What is the biggest scientific known unknown at the moment?

In our view, it is clear that immune responses of the CD4 T (intelligence service) cells and antibodies are being undermined by the evolution of the virus. It is foreseeable that this part of the immune response will be further or completely undermined by future mutations. Given the time it will take to vaccinate the world, this would appear to be more a question of when rather than if.

The biggest unknown is whether the CD8 T cells (or killer cells) will be sufficient to prevent death as antibody defences wane. We have not seen any studies that can answer this question with any certainty. We have spoken to some of the world's foremost scientists on this issue and they admit they do not know the answer.

The bet investors are making is that the killer CD8 T cells will always provide a sufficient defence even if antibodies fail to give sufficient protection. This appears to be a gamble.



## Q8. How should investors be thinking about risk in the environment?

At Magellan, we don't invest on speculation or hope but rather we invest on our assessment of the facts. We are not entrusted to speculate with your money. Our best assessment is that we need to be cautious until clearer facts emerge on the mutation risk of the virus. There is no margin for error in markets to account for this risk. We have no idea if an escape mutant will emerge. But we know this risk is foreseeable. You need to add to this risk the complexity of the macroeconomic environment driven by the massive monetary and fiscal stimulus that is being deployed and also the rising risk from emerging speculative bubbles. There are plausible and foreseeable scenarios for economic prosperity and rising stock markets and scenarios that could result in a material correction to stock markets. When you are in The Year of Living Dangerously, it's best to remember Warren Buffet's advice: "To finish first, you must first finish."

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