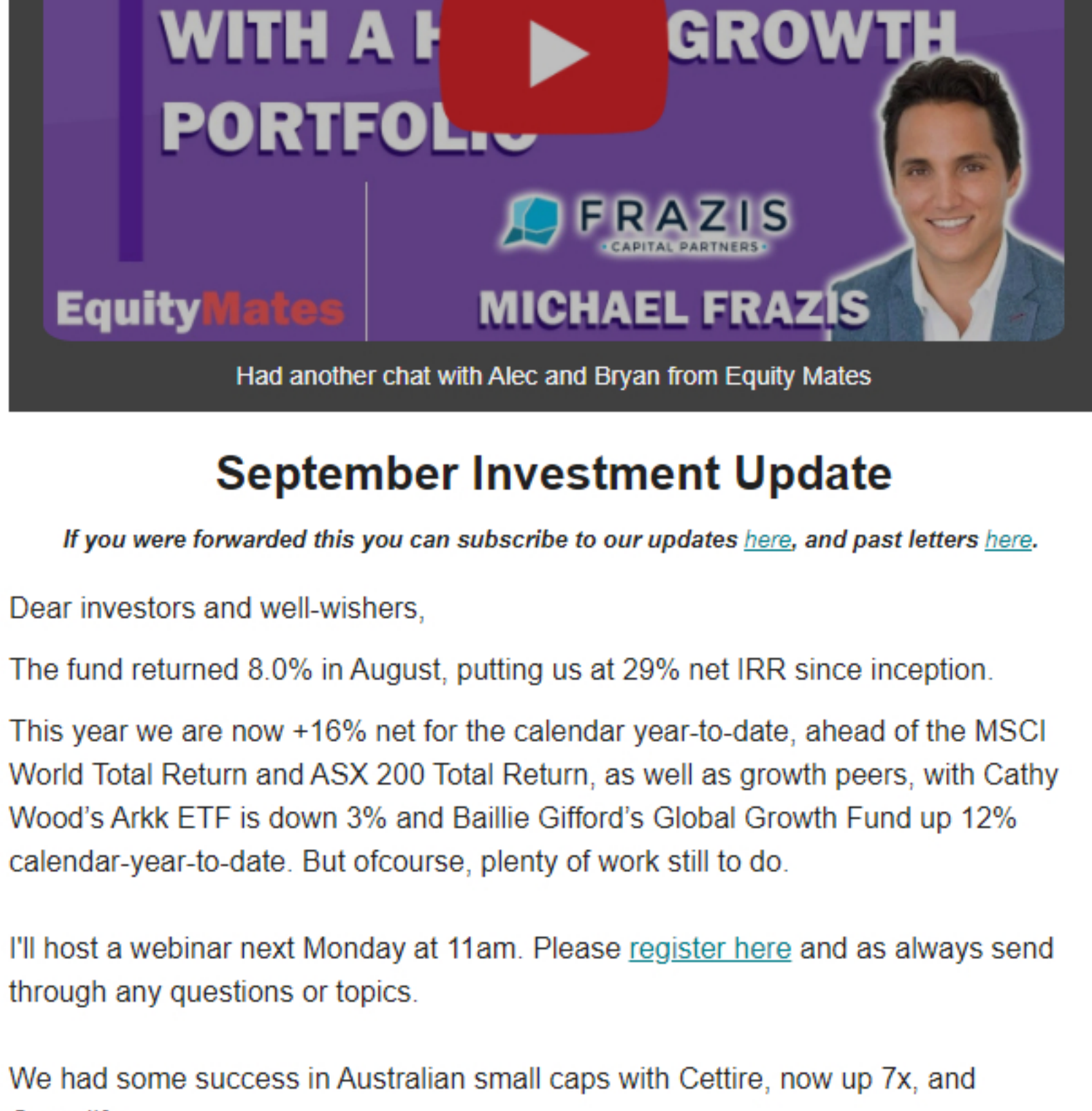


FRAZIS

• CAPITAL PARTNERS •



September Investment Update

If you were forwarded this you can subscribe to our updates [here](#), and past letters [here](#).

Dear investors and well-wishers,

The fund returned 8.0% in August, putting us at 29% net IRR since inception.

This year we are now +16% net for the calendar year-to-date, ahead of the MSCI World Total Return and ASX 200 Total Return, as well as growth peers, with Cathy Wood's Arkk ETF is down 3% and Baillie Gifford's Global Growth Fund up 12% calendar-year-to-date. But of course, plenty of work still to do.

I'll host a webinar next Monday at 11am. Please [register here](#) and as always send through any questions or topics.

We had some success in Australian small caps with Cettire, now up 7x, and Amplify:

Cettire



Amplify



These are two excellent local examples of the plentiful live opportunities that arise in markets.

The data is now out showing the mass rotation away from China ([source](#)).

Investors shift away from China

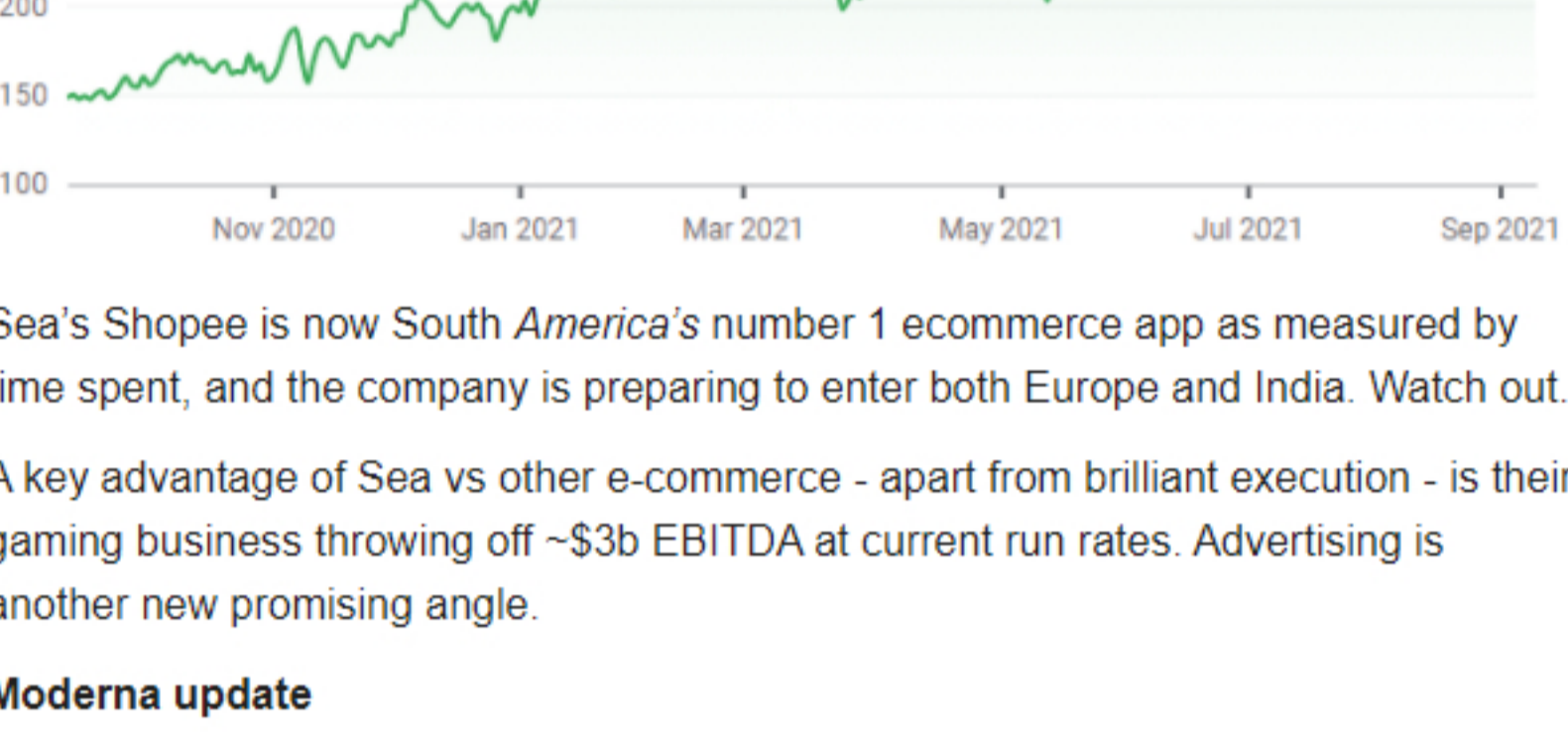
Average exposure to China and Hong Kong (%)



Based on a review of 381 global equity funds with combined assets of \$1.1tn
Source: Copley Fund Research
© FT

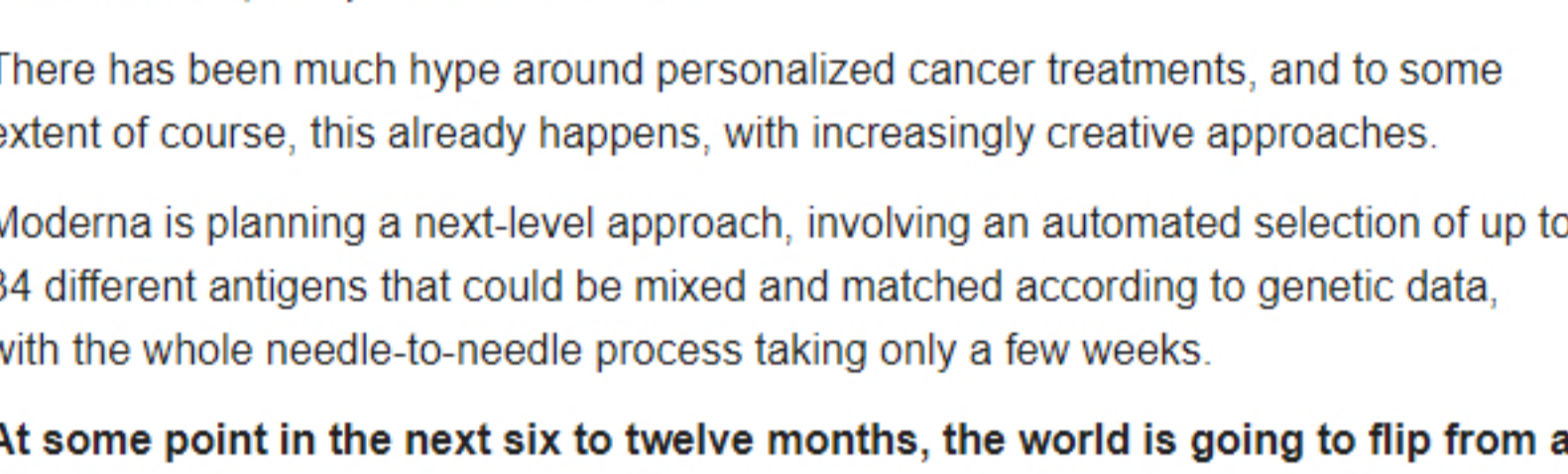
Global equity funds

Ratio of US vs China & HK holdings



Source: Copley Fund Research
© FT

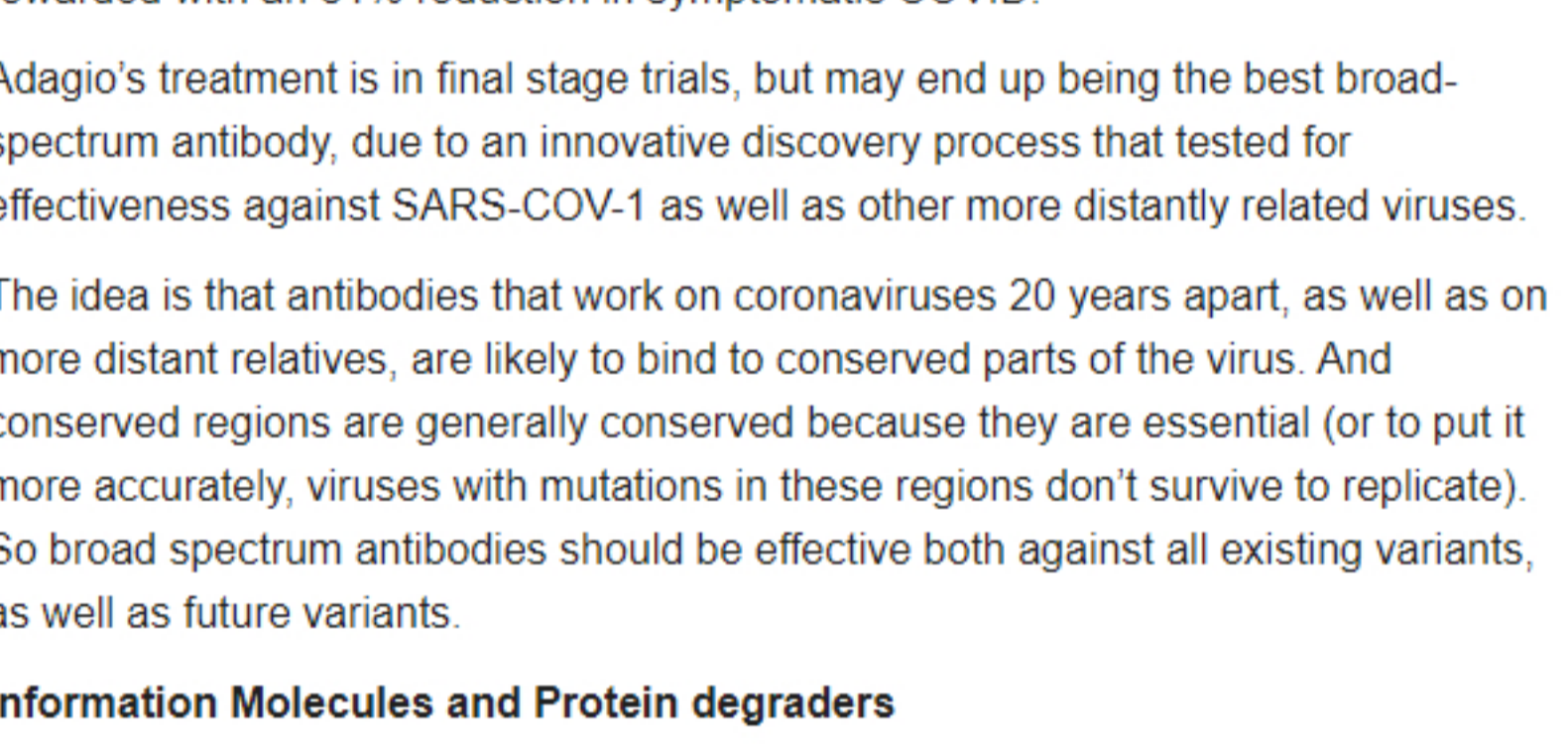
KraneShares CSI China Internet ETF



Some of our long held positions have also continued to grind higher, including Sea Ltd, which is one of the first growth stocks to push above it's February high - hopefully soon to be followed by the rest!

It's surprising to us that even now, most of our portfolio companies are still down 30% or more from their 52 week highs.

Sea Ltd



Sea's Shopee is now South America's number 1 ecommerce app as measured by time spent, and the company is preparing to enter both Europe and India. Watch out.

A key advantage of Sea vs other e-commerce - apart from brilliant execution - is their gaming business throwing off ~\$3b EBITDA at current run rates. Advertising is another new promising angle.

Moderna update

Moderna will begin trials on their two HIV vaccines this month, and the firm is so far winning the race to have a multivalent annual vaccine that would cover coronavirus strands, RSV, and influenza, which, if executed correctly, would make their current valuation cheap again.

In a recent trial, Moderna's vaccine was 84% effective at preventing breakthrough COVID cases, compared to Pfizer at 54%.

There has been much hype around personalized cancer treatments, and to some extent of course, this already happens, with increasingly creative approaches.

Moderna is planning a next-level approach, involving an automated selection of up to 34 different antigens that could be mixed and matched according to genetic data, with the whole needle-to-needle process taking only a few weeks.

At some point in the next six to twelve months, the world is going to flip from a shortage of vaccines to an overabundance, even in places like Australia (to be fair, we have been in abundance for some time now, if you include Astrazeneca).

Just now the UK Government announced the cancellation of a vaccine order with Valneva, a French firm who was developing a whole inactivated vaccine. This is perhaps a sign of things to come.

We discussed in [a recent webinar](#) that we think the next exciting development in coronavirus is actually going to be in treatments, rather than vaccines, which will remain relevant as endemic disease threatens the sick and elderly. There are a number of companies that have now developed antibodies - we have invested in Adagio and Regeneron.

If you missed it, Regeneron's randomized, double-blind, placebo-controlled trial tested 1,500 people who were recent household contacts of positive coronavirus cases. Those lucky enough to receive the antibody, rather than the placebo, were rewarded with an 81% reduction in symptomatic COVID.

Adagio's treatment is in final stage trials, but may end up being the best broad-spectrum antibody, due to an innovative discovery process that tested for effectiveness against SARS-COV-1 as well as other more distantly related viruses.

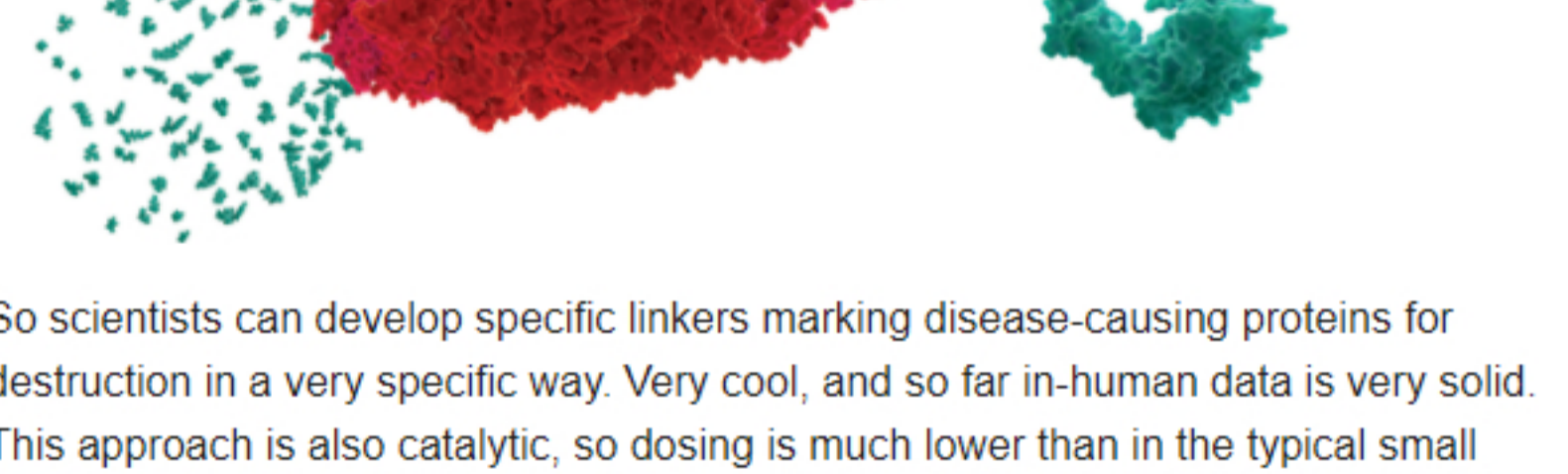
The idea is that antibodies that work on coronaviruses 20 years apart, as well as on more distant relatives, are likely to bind to conserved parts of the virus. And conserved regions are generally conserved because they are essential (or to put it more accurately, viruses with mutations in these regions don't survive to replicate).

So broad spectrum antibodies should be effective both against all existing variants, as well as future variants.

Information Molecules and Protein degraders

The most exciting developments in the life sciences right now are focused on information molecules, on mRNA, RNAi, and also the less commercially successful gene-editing techniques, like CRISPR.

Life uses a quaternary system



mRNA is an information molecule

We think this positioning from Moderna is likely to stick.

The information molecule approach is very different to traditional pharmaceuticals, which focus on small molecules that [look pretty](#) to organic chemists. But these small molecules are plagued by side effects, as when evolution stumbles on an effective receptor, it swaps, replicates, duplicates, and mutates the associated genes and uses them in all kinds of different ways. This means drugs have unintended consequences.

To block active sites effectively with a small molecule, you need to maintain consistently high concentrations to compete with the protein of interest for the active site. So dosing must be continuous.

And not have the vast majority of these disease-causing proteins are 'undruggable' - they don't sadly, an easily accessible active site or perhaps are used for some non-catalytic function like intracellular scaffolding.

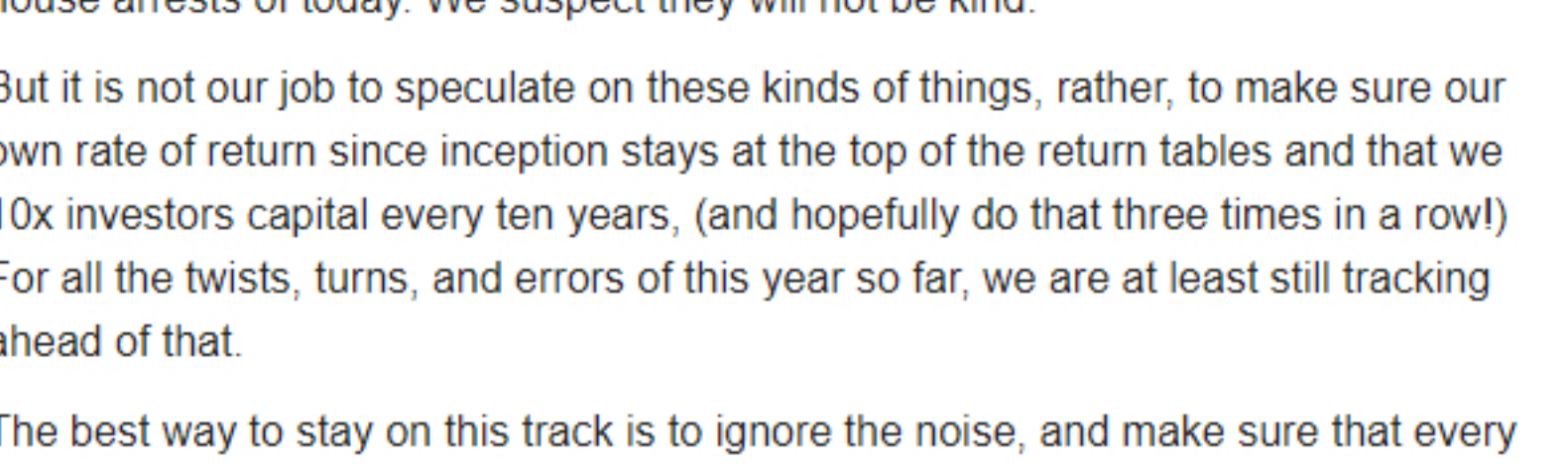
Wouldn't it be fantastic if we had a way to selectively destroy these disease-causing molecules?

As it turns out, such a mechanism exists.

Protein degraders

Our bodies constantly recycle the contents of our cells - breaking old proteins down to make new ones. A molecule called ubiquitin acts like a flag that tells the cell that this protein's time is up and it's ready to be destroyed. Since every cell in the body needs to recycle its proteins, ubiquitin is 'ubiquitous' (hence the name) in most cells and tissues. Therapeutically this means that a therapy involving ubiquitin could be targeted to essentially all tissue types.

Proteins tagged with ubiquitin are marked for destruction. The taggers, E3 ligases, are extremely varied (we have several hundred each) and can be linked with chemical glues to attach to target proteins of interest.



So scientists can develop specific linkers marking disease-causing proteins for destruction in a very specific way. Very cool, and so far in-human data is very solid.

This approach is also catalytic, so dosing is much lower than in the typical small molecule situation, as the drug can destroy protein after protein like a machine given a singular task. In contrast, a traditional small molecule drug can only 'block' one protein at a time.

If you'd like our detailed piece on this, please let me know and I'll send over our internal research notes (investors only).

This pathway is already actually used by the thalidomide class of drugs, though they predate the discovery of the mechanism. Thalidomide is that drug infamous for inducing birth defects (sadly, it was prescribed to pregnant women for morning sickness). The drug has since found extensive use in oncology, where it acts as a molecular glue fastening on to exactly this protein destruction machinery.

We have invested in the two leading companies in the space, and as with Adagio, they have already added to performance.

Opportunities

Delta has extended the pandemic, magnifying the associated economic and political impact, as well as reinforcing those new behaviours we all had to learn.

An old bug-bear of mine was that so little time and money was spent on curbing the common cold. Traditional vaccine technology were a little too slow and cumbersome to address the evolutionary velocity of respiratory viruses, but still, it was an annoying scientific blindspot. So the efforts of Moderna and other mRNA institutions are very, very welcome, with their printable approaches that can tackle new variants of all kinds of viruses at almost the speed they emerge.

This may will be the lasting scientific legacy of these times.

Though there will be others. Lockdowns are gripping the Australian polity, though the mood does seem to be changing at the margins.

The hundreds of billions spent on lockdown measures are laudable in the intent to save and extend life, but we do wonder if such funds could have been spent in more effective ways.

Historians and scientists of the future, with the distance of time and the absence of fear, will cast their verdict on the border closures, bureaucratic cruelty, and mass house arrests of today. We suspect they will not be kind.

But it is not our job to speculate on these kinds of things, rather, to make sure our own rate of return since inception stays at the top of the return tables and that we 10x investors capital every ten years, (and hopefully do that three times in a row!) For all the twists, turns, and errors of this year so far, we are at least still tracking ahead of that.

The best way to stay on this track is to ignore the noise, and make sure that every single company we own is a rockstar business, growing bigger, better and stronger every single day, and that remains as true as ever. The good news for those of us in New South Wales is there does seem to be a light at the end of the lockdown tunnel, so we will host an event for investors in Sydney as soon as regulations allow.

Best wishes,

Michael

I'll host a webinar next Monday at 11am, feel free to [register here](#) and send through any questions or topics you'd like me to address.

If you'd like to invest with us, you can access our investment portal and fund documentation through the button below, or simply reply to this email and we'll be in touch.

Please note: We are now taking applications weekly, so if applications, funds and supporting documents are received by 2pm on a Friday, the investment will be priced for Friday COB / Monday morning start. We are also available on Netwealth, Hub24, and other select platforms.

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