Weekly thoughts on the healthcare sector from finnCap's life sciences analysts: Mark Brewer and Arshad Ahad

Market	Last	-1D	-1M	-3M	-12M	YTD	Health	Last	-1D	-1M	-3M	-12M	YTD
MSCI World Index	1,543	-1.6%	2.2%	-17.4%	-3.5%	-14.3%	MSCI World Pharma/Biotech	217	0.0%	6.8%	-1.3%	19.0%	1.6%
FTSE All Share	3,171	-1.5%	0.3%	-21.8%	-17.4%	-22.7%	FTSE All Share Health	13,569	1.3%	17.8%	8.2%	30.1%	5.4%
AIM All Share	811	-0.6%	9.9%	-15.1%	-13.8%	-14.5%	**AIM Health**	10,138	0.7%	17.2%	-4.5%	-3.0%	-2.2%
AIM 100	4,145	-0.5%	9.4%	-15.1%	-15.8%	-14.7%							

- The following two tables provide the latest updates on the most promising treatments and vaccines being investigated for COVID-19.
- An archive of all previous Health Matters editions can be found here.

Treatments being investigated for COVID-19				
Company	**Drug**	**MoA / Approvals**	**Clinical trials include:**	**Comment**
Gilead	Remdesivir	Antiviral US and JP approval for COVID-19	Multiple studies, including: Phase III: Two open-label RCT's. SIMPLE I trial in 6,000 pts SIMPLE II in 1,600 pts. NIAID: Phase 2 RCT, double-blind, placebo-controlled	Received emergency use FDA authorisation on May 1. Received Japanese approval on May 11. Conflicting data: NIAID study showed improvement in disease duration, but no improvement in survival rate. Lancet trial showed no statistical clinical benefit. (See Health Matters 1st May for more information).
Roche/Chugai	Actemra (tocilizumab)	Anti-IL6R mAb Approved for RA Chinese approval for COVID-19	Phase III: COVACTA RCT for 330 pts, double-blind, placebo-controlled CORIMUNO-19: Randomized French trial in 129 pts. RECOVERY UK RCT, assessing 5 drugs in 12,000 pts	Chinese approval for treating COVID-19 patients with lung complications, stems from hope that the drug could be able to interrupt 'cytokine release syndrome' (CRS). Preliminary results from CORIMUNO-19 shows the primary endpoint was met, significantly lower proportion of pts in Actemra arm died or required ventilation.
Sanofi / Regeneron	Kevzara (Sarilumab)	Anti-IL6R mAb. Approved for RA	Phase II/III trial for severe COVID-19 patients. Multicentre, double-blind, 600 pts.	Phase II was split into 'severe' and 'critical' pt groups. Results showed negative trends in former, and positive trends in latter. However, the negative trends were not reproduced in Phase III. More data required.
AbbVie	Kaletra (Lopinavir-Ritonavir)	Antiretroviral Approved for HIV	Failed 199 pt trial in China RECOVERY UK RCT, assessing 5 drugs in 12,000 pts	One RCT among 199 pts in China found no differences in viral load or 28-day mortality. However, the same doctors reported it helped some of the COVID-19 pts they treated. Further data required.
Generic (Bayer, Mylan and Teva, Others)	Generic chloroquine and hydroxychloroquine	Anti-malarial Approved for malaria, for past 70 yrs.	Multiple, including observational study in New York, 811 pts, placebo-controlled. RECOVERY UK RCT, assessing 5 drugs in 12,000 pts	After initial hopes (including those fuelled by the US president), this drug is no longer a big contender. New England Journal of Medicine results from 811 pts showed no harm or benefit from hydroxychloroquine.
Fujifilm (but is now genericised)	Avigan (favipiravir)	Approved for flu in JP Approved for COVID-19 in China	Phase III trials in JP Phase III trial in India	Antiviral. Early data from Chinese licensee (Zhejiang) suggest a benefit in early stage disease. Glenmark Pharmaceuticals has initiated a Phase III trial in India on 12 May. JP govt considering approval for COVID-19.
Novartis and Incyte	Jakavi (ruxolitinib)	JAK inhibitor Approved to treat rare bone marrow cancers.	Phase III: RUXCOVID will assess Jakavi plus SOC versus SOC alone, in 64 pts.	Alongside trial, Incyte aims to initiate a separate open-label Expanded Access Program in the US to allow eligible pts with COVID-19 associated cytokine storm to receive ruxolitinib.
Synairgen* (AIM:SNG)	SNG001	Inhaled interferon beta	Phase II: 220 pts, double-blind, placebo-controlled trial.	Naturally occurring protein, direct delivery to the lungs via nebulisation. Addition of exogenous IFN-beta before or during viral infection of lung cells either prevents or greatly diminishes cell damage and viral replication, respectively. First data readout expected by June. (See Health Matters 1st May for more information).
BerGenBio	Bemcentinib	AXL kinase inhibitor	Phase II: ACCORD Study, 120 pts	First candidate selected to be tested in UK govt's ACCORD programme, aimed at fast-tracking potential treatments, with those showing promise progressing into larger scale studies such as RECOVERY. Bemcentinib has demonstrated promise in preclinical data against SARS-CoV-2.
Apeiron Biologics	RhACE2 APN01	Recombinant human angiotensin-converting enzyme 2	Phase II RCT in 200 pts.	Recombinant version of the rhACE2 enzyme, designed to imitate human ACE2 used by the SARS-CoV-2 virus to enter host cells.
Ono Pharma	Foipan (camostat mesilate	Protease inhibitor Approved for chronic pancreatitis in JP and South Korea	Phase I/II placebo-controlled RCT in 580 pts.	A paper in the Cell journal showed that the agent can prevent SARS-CoV-2 from entering human cells. Data from RCTs required.
NA (Non-drug therapy)	Convalescent plasma	Method has been used for over 100 years	Small trials around the world.	Blood plasma from recovered COVID-19 pts is transfused into pts who are currently ill, in the hopes that freshly-made antibodies will help fight the virus. One small pilot study in China found virus levels dropped rapidly in a trial of 10 pts, with improvements in symptoms within 3 days. Much more data needed.
Tiziana Life Sciences (AIM: TILS)	TZLS-501	Anti-IL6R mAb	Early	Anti-IL6R mAb. Dual-mechanism of action may have advantages over other anti-IL6R mAbs such as Actemra and Kevzara.

Source: finnCap. MoA= Mechanism of Action. RCT= Randomised Clinical Trial. Pts= Patients. RA= Rheumatoid Arthritis. SOC= Standard of Care.

UK RECOVERY: World's Largest Randomised Trial

- RECOVERY (Randomised Evaluation of COVID-19 Therapy) is the largest randomised placebo-controlled trial in the world, aiming to recruit 12,000 participants (9,924 have already been recruited), at over 176 NHS sites in the UK.
- The trial is evaluating five repurposed drugs: lopinavir-ritonavir, hydroxychloroquine, tocilizumab, low-dose dexamethasone (a type of steroid used in a range of conditions typically to reduce inflammation) and azithromycin (a commonly used antibiotic).
- The drugs included were based on an assessment criteria that considered drugs that had theoretical reasons to believe they may work, a known safety profile, and enough supply for a large trial.
- The trial design is dynamic, with the expectation that drugs will be added or removed as evidence changes and new candidates are developed.

Vaccines being investigated for COVID-19				
Company or Research body	Candidate	MOA	Trials	Comment
Moderna / NIAID	mRNA 1273	RNA vaccine	Phase III: Protocol being finalised Phase II: Study expected to begin shortly. 600 subjects (18-55 n=300, over 55 n=300) Phase I: 45 subjects aged 18 to 55 in 3 locations in the US	Made with mRNA encoding the spike protein on the surface of SARS-CoV-2. Delivered via a lipid nanoparticle. Phase I trial completion estimated 1 June. Moderna received US federal funding worth up to $483m to accelerate development of its vaccine. Phase III expected to begin early summer.
Cansino Biological Inc.	AD5-nCOV	Non-replicating viral vector expressing SARS-CoV-2 spike protein	Phase II: 500 subjects (18 to 60 years) Phase I: 108 subjects (18 to 60 years)	Genetic engineered vaccine with the replication-defective adenovirus type 5 as a vector to express the SAR-CoV-2 spike protein. Decision to advance to Phase II was made based on unreleased preliminary safety data from Phase I trial.
University of Oxford	ChAdOx1	Non-replicating viral vector	Phase I/II: 1,119 subjects (18 to 55 years) at four centres in the UK	Based on non-replicating, attenuated chimpanzee adenovirus vector and the SARS-CoV-2 spike protein. Data could be available in 2-6 months.
Biontech / Pfizer	BNT162	RNA vaccine	Phase I/II: 360 subjects, two age cohorts (18-55 and 65-85)	The programme includes four candidates, each representing a different combination of mRNA format and target antigen, and the design of the trial allows for evaluation of the candidates simultaneously.
Shenzhen Geno-Immune Medical Institute	LV-SMENP	Lentiviral minigene vaccine	Phase I/II: 100 subjects in Shenzhen, China.	Engineered minigenes encoding viral antigens; lentiviral vector designed to infect dendritic and T cells, which are key components of the immune system, to induce immunity. Trial expected to complete by July 31.
Murdoch Childrens Research Institute	BCG tuberculosis vaccine	Administered BCG	Phase I/II: 100 subjects (6 months to 80 years).	Bacillus Calmette-Guérin tuberculosis vaccine that induces a broad innate immune-system response, which has been shown to protect against infection or severe illness with other respiratory pathogens.
Inovio Pharmaceuticals	INO-4800	DNA plasmid vaccine	Phase I: 40 subjects (18 to 50 years).	DNA plasmid vaccine delivered through the skin via a patch-style device using a brief low-voltage electronic pulse to induce cell membranes to open, making them more receptive, in theory, to accepting the vaccine's genetic material. Preliminary data expected by late summer.
Novavax	NVX-CoV2373	Stable prefusion protein	Preparing to initiate Phase I trial in around mid May.	Proprietary Matrix-M adjuvant will be incorporated with the candidate in order to enhance immune response. Strong immunogenicity in animal tests.
Sanofi/GSK	Multiple	Multiple	Plans to start trials H2 2020	In mid-April, two of the world's largest vaccine manufacturers announced unprecedented collaboration to test six candidates built on technologies already proven in flu vaccines. In all candidates, Sanofi's recombinant S-protein COVID-19 antigen will get a boost from GSK's AS03 adjuvant.

Source: finnCap, mRNA= Messenger Ribonucleic acid. NIAID= US National Institute of Allergy and Infectious Diseases.

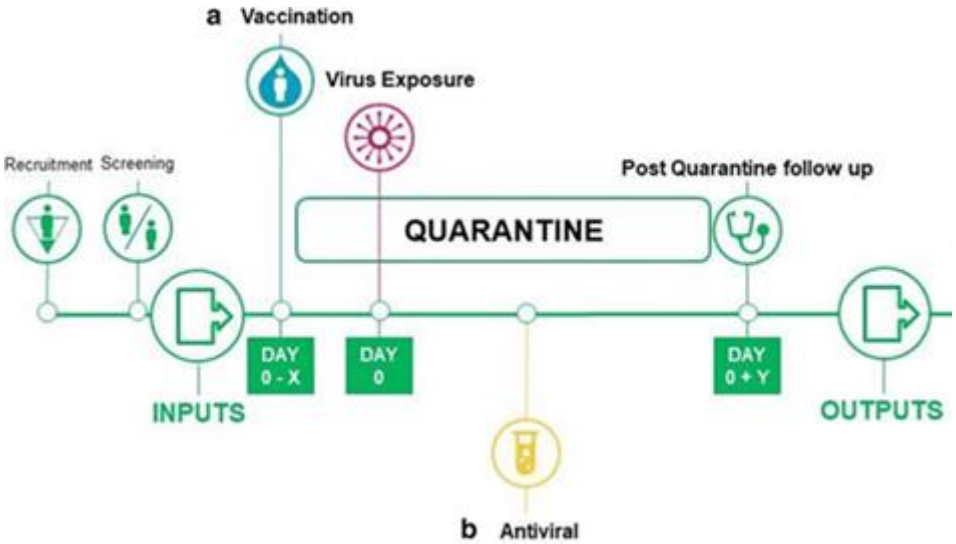
Open Orphan*: Developing the World's first COVID-19 Challenge Model

- On May 11, finnCap was appointed as joint broker to Open Orphan (AIM: ORPH). As discussed in Health Matters May 1, Open Orphan can expedite the **testing of vaccines and antivirals** against COVID-19.

- Its subsidiary, hVIVO is the world leader in the provision of **challenge studies**, which involve **deliberately infecting** healthy volunteers with an infectious disease, while in **quarantine**, and then returning them to healthy.

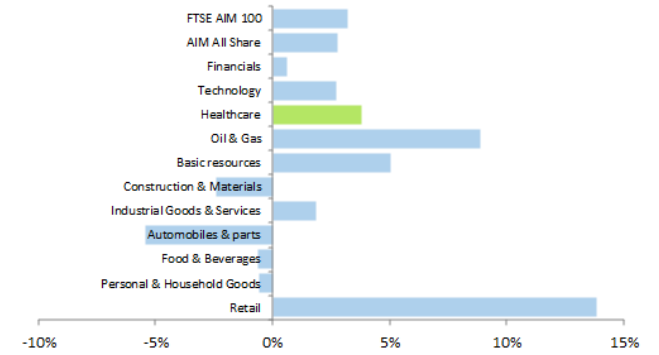
- Challenge studies can greatly **fast track** testing, with **reduced costs** and **fewer volunteers** required. And unlike conventional Phase I studies, challenge studies include valuable efficacy endpoints that guide decisions on how to optimise subsequent field studies.

- For comparison, it is unknown whether the **ChAdOx1 Oxford trial** will take **2 months** or **6 months**, and this is because it is necessary for a number of the study participants to naturally become infected with COVID-19, and the time required for this to happen **cannot be predicted**. Timing will depend on levels of viral transmission in the community. The trial lead stated: "We are **chasing the end** of this current epidemic wave, if we don't catch that, we **won't be able** to tell whether the vaccine works in the next few months".



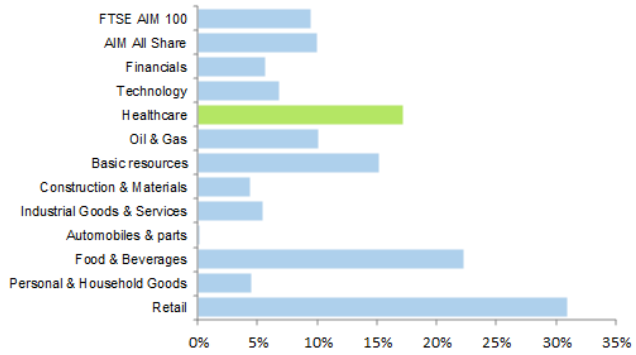
A human viral challenge model. Source: Respiratory Research

FTSE AIM all share sector performance (1 week)



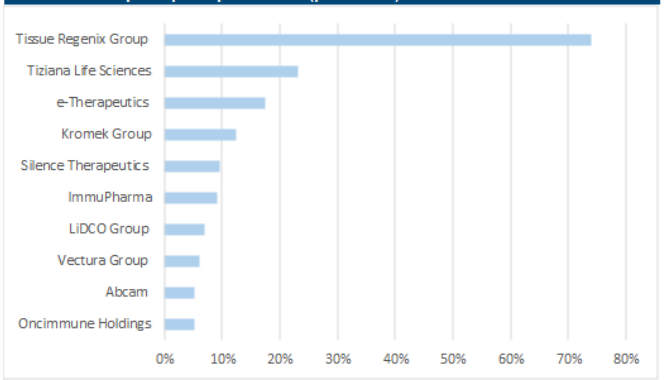
Source: FactSet

FTSE AIM all share sector performance (1 month)



Source: FactSet

finnLife 50 - Top ten price performers (past week)



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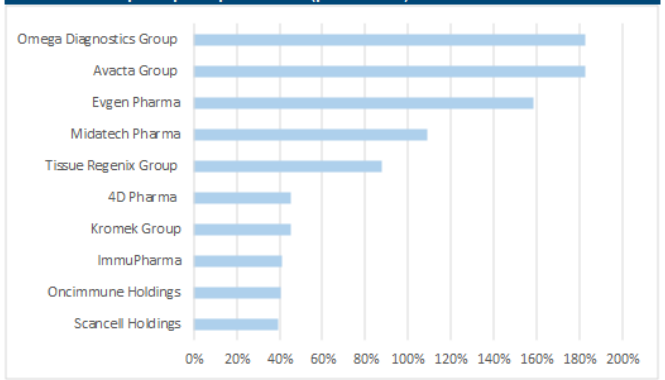

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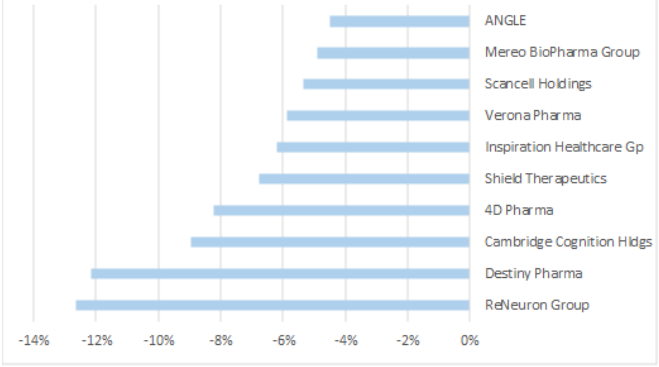

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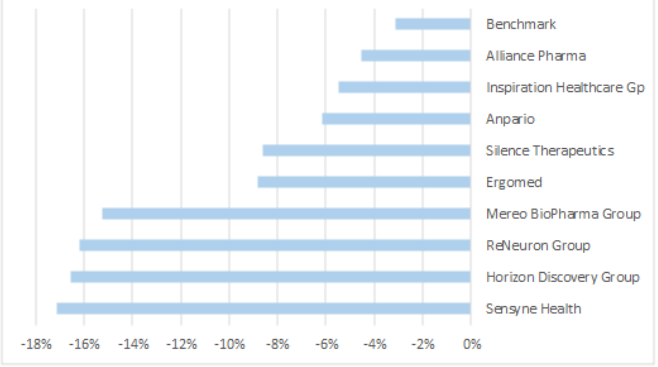

Source: FactSet

Research reports and comments in the past week

Company	Date	Title	Research Type
Avacta*	11 May	COVID-19 rapid antigen test – update	Morning Note
Genedrive*	12 May	£7m placing to fund COVID-19 tests	Company Note
ANGLE*	12 May	Peer-reviewed paper demonstrates Parsortix utility	Morning Note
Oncimmune*	12 May	Drug development collaboration with US biopharma	Morning Note
Byotrol*	14 May	A pair of licences and a positive trading update	Company Note

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The recommendation system used for this research is as follows. We expect the indicated target price relative to the FT All Share Index to be achieved within 12 months of the date of this publication. A 'Hold' indicates expected performance relative to this index of +/-10%, a 'Buy' indicates expected outperformance >10% and a 'Sell' indicates expected underperformance of >10%.