DEVON Equity Management

Global Opportunities Fund: Investment Letter – Q2 2021

The Fund returned 16.2% in the quarter.[1]

In light of three important yet mutually exclusive developments during the quarter, this letter is devoted to the healthcare and life sciences sector:

Next Generation Sequencing (NGS)

At the ASCO Meeting in early June, **GRAIL** released interim results from the PATHFINDER Study. Recall **Illumina (5.6% of NAV)** are in the process of acquiring GRAIL for US$8bn (discussed in our Q4 2020 Investment Letter).

The PATHFINDER Study assesses the performance of *Galleri*, an early detection test for up to 50 different types of cancer. The Study delivered 45% positive predictive value (PPV), meaning if a positive test result were returned there was a 45% likelihood the patient had cancer.

Whilst 45% might seem a relatively 'low' level of accuracy, the results were received positively, since absent the Galleri test many of these cancers are likely to have gone undetected (given a lack of alternative testing or diagnostics).

The Galleri Test is now available on prescription in the US, and GRAIL have commenced a real-world Study in a much larger US patient population (in addition to a sizable trial with the NHS in the UK).

In the race to develop broad based early stage cancer detection tests, from an operational perspective GRAIL is clearly exhibiting impressive progress. Frustratingly, Illumina's acquisition of the company has been complicated by regulatory intervention in both the US and EU.

In a surprise move, the US Fair Trade Commission (FTC) moved to block the merger on competition grounds. Illumina will vigorously contest the FTC's move in the courts. Illumina / GRAIL represents a 'vertical' acquisition, where the FTC has historically taken keener interest in 'horizontal' acquisitions (such as Illumina's unsuccessful attempt to acquire Pacific Biosciences in 2019). The last major vertical acquisition contested by the FTC was AT&T / Time Warner in 2019. In this case the FTC was unsuccessful, as they failed to offer factual arguments as to how the merger would decrease competition in the Pay TV market. The merger duly closed. This brings us to the heart of why the FTC challenge came as a surprise in the Illumina / GRAIL case.

Blocking a deal on competition grounds when the acquiree company (GRAIL) does not have any revenue, and the market which they are targeting barely exists seems a surreal concept. Effectively, the FTC will need to prove Illumina's acquisition of GRAIL will be anti-competitive in a market which doesn't really exist.

The FTC's concern centres on the dependency of other liquid biopsy players on Illumina's sequencing machines to read samples. Illumina's binding commitments to lower sequencing costs to <u>all</u> liquid biopsy players by at least 45% over the coming years would appear to weaken the FTC argument that this acquisition could lead to price increases for non-GRAIL liquid biopsy players.

The EU's intervention came as even greater surprise, as GRAIL neither generates revenue nor has any physical operations within the European Union. Even for the incumbent EU Competition Commissioner (whose track record illustrates a desire to intervene in anything and everything), this looks like severe regulatory over-reach.

[1] 31st March 2021 – 30th June 2021 (net of all fees and expenses).

Considering the merits of the FTC / EU's case, we think Illumina is likely to prevail. Having said this, we fully appreciate regulatory outcomes can be unpredictable (and influenced by political / ideological agendas at the respective regulatory agencies). In the event the deal is blocked we remain comfortable with Illumina's prospects on a standalone basis.

As a final word on Sequencing – we established a position in Pacific Biosciences (PACB US) during the quarter. Pac Bio are the leader in Long Read Sequencing (Illumina are dominant in Short Read). The Long Read market is far less developed than short read, but our continued research into the genomic sequencing field increased our confidence in the commercial viability for Long Read Sequencing in the coming years. We will discuss the investment case for Pac Bio in more detail in a future letter.

Alzheimer's Disease (Eli Lilly – 3.8% of NAV)

In one of the most controversial moves in its long history, the US FDA approved Biogen's (BIIB US) Alzheimer's drug *Aducanamab* for commercial usage. The background is complicated and beyond the scope of this letter, but the controversy centres on both the interpretation of clinical trial data and the efficacy of the drug itself. The ultimate surprise came in June, when the FDA approved *Aducanamab* for commercial use with generous labelling (until at least 2030) in direct contradiction to the recommendation of the FDA's own Advisory Committee of experts (AdCom), who in December 2020 voted against approval by 10 to 0 (with one abstention).[2]

The decision caused a storm of criticism from clinicians and triggered a wave of resignations from members of the AdCom who had issued the original judgement (though 'advisory', the views of these expert panels typically carry enormous weight with the FDA).

Shortly after approving *Aducanamab*, the FDA offered breakthrough designation to Eli Lilly's Alzheimer's drug *Donanemab*, which published encouraging Phase II trail data in February 2021.[3] Breakthrough Designation opens a path to accelerated approval based on the existing clinical trial data, whereas the expectation was for an additional 2-year Phase III clinical trial to be necessary before filing for commercial launch.

Whilst the FDA's stance in favour of both drugs is highly controversial (especially Biogen's *Aducanamab)*, it reflects the scale of unmet need: Alzheimer's has a huge global patient population and total lack of approved therapies.

The FDA's accommodative stance towards these two drugs (both of which target the same 'amyloid plaque' clearance approach) is also likely to be motivated by the relatively mild side effects. From the perspective of most patients (and at least a certain cohort of physicians), a generally well-tolerated drug which might help slow the progression of such a debilitating disease represents a compelling proposition (and crucially favourable 'risk/reward').

Though Alzheimer's is probably the biggest unmet clinical market (potential TAM in the tens of billions of dollars globally), considering the controversy around both the efficacy of these drugs and the approval mechanism the addressable market in the first instance will be a sub-segment of patients (almost certainly confined to the US).

Our core thesis on Eli Lilly rests on diabetes and obesity, where they represent one half of a quasi-duopoly (along with Novo Nordisk, the largest holding in Devon's European Funds).

Given Lilly's long, expensive, and largely unsuccessful history with Alzheimer's drugs – prior to the Phase II data for *Donanemab* released in February we considered it an 'option' within an outstandingly strong drug discovery pipeline.

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[2] Vote count refers to the results of the 4th of 4 questions posed to the Advisory Committee on November 6th 2020.
[3] Eli Lilly & Co Press Release (24 June 2021).

Given blockbuster potential, clearly the FDA's stance is a significant positive to the thesis (reflected in Lilly's 37% return YTD). Having said this, we continue to view the path to commercial success for *Donanemamab* as long and fraught with potential roadblocks.

With this in mind, we remain most excited about *Tirzepitide:* Lilly's GLP/GIP dual agonist to treat diabetes and obesity. Amidst the Alzheimer's melee, we have also seen the results of four late-stage clinical trials for *Tizepatide* this year, which we think confirm the drug's potential as a clear best-in-class molecule in Lilly's most important franchise.

Thermo Fisher / PPD

The broad response to the COVID pandemic from the healthcare, pharmaceutical, and life science industries has been nothing short of incredible.

Whilst Vaccine makers understandably garner the highest profile, Thermo Fisher (6.2% of NAV) should be considered one of the outstanding performers, reflected in their *'COVID related revenue'* hitting US$9.4bn in the 12 months since March 2020 (we appreciate measuring 'contribution' to the pandemic by 'dollars' generated is a little crude – but ultimately it does tell us something).

Ever the short-termist, Mr Market has looked to the inevitable slowdown in COVID related revenue uneasily – questioning whether it might mean a decline in Earnings come 2022. These concerns resulted in TMO shares declining 5% since their November 2020 peak[4], the worst performer of our Top 10 holdings.

Fortunately, we look at the COVID dynamic for Thermo in the diametrically opposite fashion.

We think Thermo's response to COVID has bolstered their competitive positon in multiple verticals, and meaningfully enhanced the long term earnings potential of the company:

Firstly, Thermo came from 'also-ran' to leading player in diagnostic testing in 6 months. In ordinary times, this might be expected to take 5+ years. As demand for COVID testing inevitably declines, the capacity Thermo built during 2020 will be filled with demand from non-COVID diagnostic tests, a fast growing area before the pandemic with improved prospects in light of the role testing is playing in the COVID response.

Secondly, Thermo invested heavily throughout 2020 in capacity for the core bioreactor business. Given our constructive view on biologics manufacturing (both volume and value), these investments should translate into sustainably higher market share.

Thirdly, we expect the ~US$4bn of 'excess' free cash flow generated from COVID related business to be reinvested into high returning businesses with a more sustainable earnings profile. This is already evident in Thermo's strong M&A activity YTD, culminating in the US$20bn acquisition of PPD (PPD US).[5]

PPD is a top tier CRO (Contract Research Organisation) which has been in and out of private equity ownership in recent times. To oversimplify, CRO's effectively provide 'outsourced' R&D services across the entire customer spectrum (from big pharma to early stage biotech). Their value proposition varies slightly be customer, but ultimately comes down to quality of drug discovery / development and accelerating time to market (i.e. 'Return on R&D investment'). CROs must stack up well on this metric vs in-house R&D spend, otherwise Firms would simply keep the spend 100% internal.

[4] Trough -18% in early June, followed by a strong rally.

[5] $20bn Enterprise Value: Announced 15th April 2021, expected to close by year end.

In the past Marc Casper (Thermo's CEO) has been publically sceptical of moving into the CRO market – the simple logic being the creation of an integrated CRO/CDMO[6] would bring Thermo into more direct competition with some of their large customers. However the acceleration in R&D spending from big pharma and explosion of innovative R&D activity in well-funded earlier stage Biotechs has driven a boom in the CRO market. COVID and the therapeutic / vaccine responses has added a further leg to the story, and the value proposition of top tier CRO's has never been stronger.

From a regulatory perspective, one might also point to the relative ease for Thermo to execute a US$20bn CRO acquisition given this is essentially a 'vertical' rather than 'horizontal' move. Since Thermo are Top 3 in the majority of their segments, any further consolidation of direct competitors in an existing business of comparable size to PPD could prove problematic. Though PPD is 'vertical' – we can clearly see synergies with Thermo's existing businesses, especially in CDMO and clinical trial drug provision / services. The targeted synergies announced in April feel highly conservative, and combined with the obvious potential for accelerated top line performance at PPD once in the Thermo stable, we expect the deal to prove far more accretive on a 3-5 year view than the ~8% earnings accretion based on publicly stated 2022 targets.

Thermo Fisher (and Danaher) have built highly successful multi-brand life science conglomerates, with M&A a critical driver of success. Our confidence in Thermo's management team to reinvest a large portion of free cash flow into M&A at high rates of return is a key facet of our investment thesis. Done well, inorganic growth can be disproportionately accretive since consensus expectations rarely capture acquisitions as a source of future earnings (even in a demonstrably acquisitive business model such as this).

We established Thermo as a Top 5 position at the Fund's inception to reflect the company's strong positioning across a number of attractive life science verticals, with Biopharma and Clinical representing ~70% of end market exposure. We are also attracted to a business model delivering strong and consistent free cash flow generation underpinned by over 50% of revenue derived from consumables.

Given the Fund's largest position (IQVIA) is a major competitor to PPD, it should come as no surprise we are excited at the prospect of Thermo's move into the CRO market – in our view one of the most attractive areas of healthcare. Thinking about possible implications for IQVIA, we are not overly concerned about market share loss over the medium term. The CRO market remains fragmented, and we think IQVIA (standalone) and PPD (under Thermo ownership) represent two of the top tier players who are likely to gain market share from second and third tier players.

Thermo Fisher trades on 22x Forward Earnings with a Free Cash Flow Yield in excess of 4%[7]: cheap vs its own history, closest comp Danaher, and the broader life science tools sector. We are comfortable with the possibility of a modest earnings decline in 2022 – to us it would be a reflection of the extent of their successful response to COVID. Recent developments give us increased confidence in the five year earnings and free cash flow prospects for the company.

[6] CDMO (Contract Development & Manufacturing Organisation) - a core Thermo business via the acquisitions of Patheon (2017) and Brammer Bio (2019).
[7] Proprietary Devon Estimates.

Investment Outlook

At time of writing, February's trading activity in the portfolio appears timely – with strong contribution from both new positions (notably **Nvidia** with a 44% return[8]), and those existing positions to which we added (Cadence, Synopsys, Hoya, Keyence, Accton).

During Q2 we participated in the IPO of **Darktrace** (3.5% of NAV), and established positions in **Pacific Biosciences** (1.5% of NAV), **Adyen** (1.2% of NAV), **Paypal** (1.9% of NAV) and **Altium** (1.9% of NAV)[9].

Five new investments is more than you should expect from us in any given quarter, though if we consider the nature of these businesses (1x Cybersecurity; 1x Genomic Sequencing; 2x Payments; 1x EDA) – they represent industries with strong existing representation within the portfolio, which should reassure these are not an indication of any change in direction, rather serve to reinforce core characteristics.

Ultimately the number of new investments during the quarter should be read as an indication of the strength and depth of opportunities we see in our expanding investment pipeline.

Charlie Southern

7th July 2021

[8] Return on Investment to 30th June 2021 (2.8% of NAV).

[9] Position Sizes as of 30th June 2021.

Global Opportunities Fund: Key Statistics

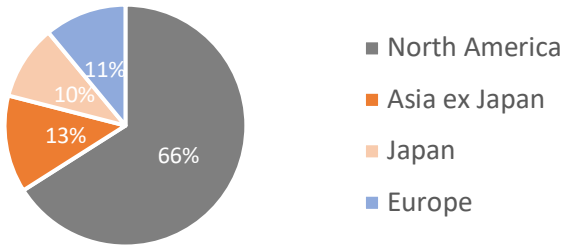
Performance

	2021 YTD[10]	2020[11]	1 Year	3 Year	5 Year	Since Inception[12]
Fund[13]	14.1%	14.6%				30.8%
Benchmark[14]	12.3%	11.9%				25.6%
Relative	*+1.8%*	*+2.8%*				*+5.2%*

Liquidity

Market Cap	No. of Positions	% of NAV	ADV
Small (< US$1bn)	0		
Mid (< US$20bn)	8	14%	US$45mn
Large (> US$20bn)	19	60%	US$375mn
Mega (> US$200bn)	8	26%	US$1,690mn
Total	**33**	**100%**	
NAV Weighted Average	US$130bn		US$615mn
Median	US$73bn		US$266mn

Geographic Allocation



Top 10 Holdings

Company	Country	% of NAV
IQVIA Holdings	US	6.9
Cadence Design	US	6.7
Thermo Fisher Scientific	US	6.2
Illumina	US	5.6
Moody's	US	5.1
SK Hynix	S. Korea	4.0
Eli Lilly	US	3.8
Darktrace	UK	3.5
Keyence	Japan	3.0
IHS Markit	US	3.0

[10] NAV: 30th June 2021 (Source: JP Morgan)
[11] NAV per share, Net of all fees and expenses: 4th November – 31st December 2020 (Source: JP Morgan)
[12] NAV per share, Net of all fees and expenses: 4th November 2020 – 30th June 2021 (Source: JP Morgan)
[13] NAV per share, Net of all fees and expenses
[14] MSCI AC World Net Total Return in USD (NDUEACWF Index)

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