12 January 2024

UK pharma vs. NASDAQ Biotech

Source: Refinitiv

HARDMAN & CO HEALTHCARE INDEX

2023 – Capital demands dent performance

The Hardman & Co Healthcare Index (HHI) has been running since 2009. Its main function is to highlight the attractions of life sciences investments over the long term. For the second year running, apart from global economic influences affecting world markets, performance in 2023 was dented by the capital-intensive nature of the sector. The HHI fell 3.7%, to 483.8, underperforming the main London markets – FTSE 100 (+3.8%) and FTSE All-Share (3.8%) but outperforming the FTSE AIM All-Share Index (-8.2%). Only 15 companies in our index saw share prices rise in 2023, four of these benefiting from trade sales. Despite challenges in raising new capital from the market, 15 companies (29%) did achieve successful outcomes. A number of companies are short of cash and will need more capital in order to get auditors to sign off their accounts – so 2024 looks as though it will be busy again.

- Despite setbacks over the past two years, since inauguration in 2009, the CAGR for the HHI has been 12.0%, compared with 3.3% for the FTSE All-Share Index and 0.5% for the FTSE AIM All-Share Index, highlighting the attractiveness of the healthcare sector as a long-term investment, despite being capital-intensive.

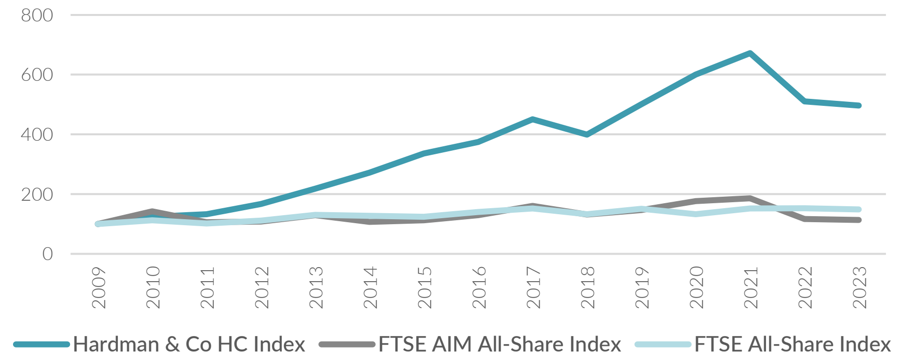
- Of the 52 companies included in the HHI, only 15 recorded an increase in their share prices in 2023, four benefiting from M&A activity. One marked time (change <0.5%) and the remaining 36 companies recorded falls.

- The variance between the best- and worst-performing stocks was in line with historic data, at 223% – hVIVO (HVO) rising 138% and Advanced Oncotherapy (AVO) down 86% at the time of being suspended; the median share price change was -20%.

- In relative terms, 17 stocks outperformed the index during 2023, with the other 35 underperforming.

- After two really good years in 2020 and 2021, biotech and healthcare stocks had become overvalued, as evidenced by a marked reduction in M&A activity. Since then, along with global markets in general, biotech and healthcare stocks have been re-rated downwards. In addition, the trend towards greater risk-aversion in response to geopolitical events, higher inflation and higher interest rates have made it more difficult to raise capital over the past two years.

Performance of Hardman & Co Healthcare Index – rebased



Source: London Stock Exchange, Hardman & Co Life Sciences Research

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Specific comments have been made in this report on the following companies

Share price performance of stocks in HHI

Listing	Company	Ticker	Share price (p) 31 Dec 2022	Share price (p) 31 Dec 2023	Market cap (£m) 31 Dec 2023	Price change (%)
NASDAQ	Abcam	ABCM	[+]15.6	[+]24.0	4,472.6	54%
AIM	Advanced Medical Soln	AMS	259.0	207.5	451.0	-20%
AIM	Advanced Oncotherapy	AVO	13.5	1.9	10.3	-86%
AIM	Allergy Therapeutics	AGY	6.3	2.5	119.2	-60%
AIM	Alliance Pharma	APH	53.0	40.5	218.9	-24%
AIM	Angle	AGL	50.5	11.8	30.6	-77%
AIM	Arecor	AREC	240.0	182.5	55.9	-24%
Main	Arix Bioscience	ARIX	107.5	126.0	162.8	17%
Main	Assura	AGR	54.6	48.1	1,429.9	-12%
AIM	Avacta	AVCT	115.0	116.5	330.4	1%
AMS	BenevolentAI	BAI	[++]3.49	[++]1.08	114.1	-69%
AIM	Camb. Nutritional Sciences	CNSL	3.8	2.4	5.7	-36%
Main	ConvaTec	CTEC	232.6	244.2	5,005.6	5%
AIM	Creo Medical	CREO	25.3	46.0	166.2	82%
AIM	Deltex Medical Group	DEMG	1.0	0.2	2.8	-85%
AIM	Destiny Pharma	DEST	53.5	70.0	66.1	31%
AIM	Eco Animal	EAH	101.0	108.5	73.5	7%
AIM	EKF Diagnostics	EKF	50.0	31.7	144.0	-37%
AIM	Ergomed	ERGO	1,272	1,350	703.1	6%
AIM	e-Therapeutics	ETX	16.5	8.2	48.1	-50%
AIM	Futura Medical	FUM	51.2	25.5	76.9	-50%
AIM	Genedrive	GDR	11.0	8.1	9.9	-26%
Main	Genus	GNS	2,984	2,170	1,432.9	-27%
AIM	hVIVO	HVO	10.0	23.8	161.6	138%
NASDAQ	Immunocore	IMCR	57.1	68.6	2,661.5	20%
AIM	ImmuPharma	IMM	1.8	1.7	7.0	-9%
Main	Indivior	INDV	1,852	1,185	1,618.1	-36%
Main	IP Group	IPO	55.8	58.1	602.3	4%
AIM	Ixico	IXI	25.5	12.5	6.0	-51%
AIM	NIOX Group	NIOX	36.5	67.0	281.9	84%
AIM	Novacyt	NCYT	113.0	61.5	43.4	-46%
Main	Oxford BioMedica	OXB	442.5	220.0	213.0	-50%
AIM	Oxford Metrics	OMG	107.5	107.0	140.6	0%
AIM	Oxford Nanopore	ONT	246.5	208.2	1,788.2	-16%
Main	Primary Health Properties	PHP	110.8	103.8	1,385.5	-6%
AIM	Proteome Sciences	PRM	3.5	4.5	13.4	29%
AIM	Redx Pharma	REDX	64.5	22.0	85.6	-66%
AIM	ReNeuron	RENE	8.8	3.5	2.0	-60%
AIM	Sareum	SAR	82.5	59.5	41.8	-28%
AIM	Scancell	SCLP	24.8	10.5	97.4	-58%
AIM	SDI Group	SDI	151.0	87.5	91.1	-42%
AIM	Shield Therapeutics	STX	7.1	6.7	52.4	-5%
NASDAQ	Silence Therapeutics	SLN	[+]15.3	[+]18.0	519.2	18%
Main	Smith & Nephew	SN.	1,110	1,078	9,415.2	-3%
Main	Spire	SPI	228.0	226.5	915.3	-1%
AIM	Surgical Innovations	SUN	1.6	0.6	5.6	-63%
AIM	Synairgen	SNG	13.5	6.0	12.0	-56%
Main	Syncona	SYNC	181.0	123.4	819.3	-32%
AIM	Tissue Regenix	TRX	57.0	52.0	36.6	-9%
AIM	Tristel	TSTL	390.0	460.0	218.1	18%
AIM	ValiRx	VAL	14.0	5.9	6.9	-58%
AIM	Venture Life	VLG	36.5	33.5	42.4	-8%

**Client of Hardman & Co*
***Share price at time of suspension; [+]USD; [++]EUR*
Source: Company data, Hardman & Co Life Sciences Research

Hardman & Co Healthcare Index

Review of 2023

HHI comprises 52 stocks…

The main function of the HHI is to monitor the performance, and to highlight the attractiveness, of life sciences investments over the long term, and to try to identify those stocks that have disruptive technologies that consistently allow them to outperform both the index and the markets. Many of the 52 constituents of the index are high-risk, still being in the development stage, with micro-capitalisations and a long way from profitability. Despite this, some companies can still make extremely attractive returns for investors. However, although pharmaceutical, biotech and healthcare industries have defensive qualities, they are not immune from global economics.

…with disruptive technologies that should allow them to outperform index and markets

Healthcare not immune to global economic pressures and events…

Furthermore, the development and commercialisation of new drugs and medical technologies is capital-intensive. Given the interlink between inflation and interest rates, coupled with the increased risk-aversion of investors since the middle of 2022, there has been a financing crunch, which particularly affects smaller companies at the earlier stages of drug discovery and development with less robust financial profiles.

…and is capital-intensive

Performance of world markets

Recent inflation data suggested that interest rates have peaked…

To put the performance of our, largely, small UK healthcare stocks into perspective, it is sensible to look first at the performance of the major world markets. The latest inflation data led investors to believe that the major central banks have finished raising interest rates, so they began betting that cuts would commence early in 2024. This generated a significant rally in global stock markets during the last two months of 2023. Comments by the Federal Reserve boosted the view that borrowing costs would fall and resulted in the S&P500 index rising 24.2% on the year. However, it should be noted that this US index is driven by the performance of a few tech stocks – Alphabet (GOOG), Amazon (AMZN), Apple (AAPL), Meta (META), Microsoft (MSFT) and Nvidia (NVDA) – all of which have been very strong.

…leading to a two-month rally in share prices

The MSCI world ex-US index, increased by a more balanced 10.3% in 2023, whereas the FTSE 100 Index, which is dominated by well-capitalised oil and gas, mining and pharmaceutical companies, increased just 3.8% over the year. This was following a year of strong outperformance in 2022 and reflected lingering concerns about comments from the Bank of England about interest rates and uncertainty about the rate of decline in the inflation rate. This FTSE 100 performance was mirrored by the much broader-based FTSE All-Share Index. In contrast, the FTSE AIM All-Share indices fell 8.2%.

2023 market performance

Index	Ticker	31 Dec 2022	31 Dec 2023	Change
S&P 500	GSPC	3,839.5	4769.8	+24.2%
MSCI All-World (ex-US)	DBAW	27.38	30.21	+10.3%
FTSE 100	FTSE100	7,451.7	7,733.2	+3.8%
NASDAQ Biotech	NBI	4,199.6	4370.6	+4.1%

Source: LSE, Refinitiv, Hardman & Co Life Sciences Research

Performance of HHI

Gut feeling that 2023 was poor for healthcare companies

Prior to compiling all the data following the close of business on the last trading day of the year, my instinct was that 2023 had been a poor year for healthcare, largely because of investors' increased aversion to risk in a higher interest rate, higher inflation economy. So, was my instinct correct?

HHI down 3.7%...

...despite benefiting from three major trade sales

In 2023, the HHI, dominated by small UK-based companies, fell 3.7%. This was following the exceptional correction (-24.1%) seen in 2022. The performance would have been much worse if it had not been for four trade sales that were concluded in 2023, of which three were significant.

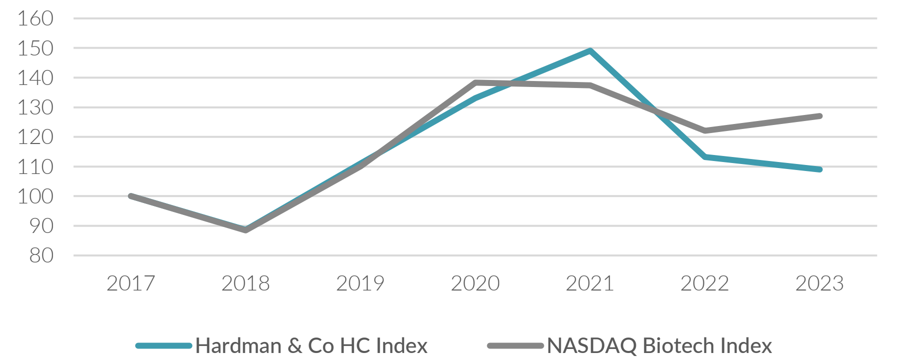
Significant sector M&A activity in 2023

Company	Acquiror	Consideration	*Uplift
Abcam	Danaher (DHR)	£4.5bn	+51%
Emis	Unitedhealth Group (UNH)	£1.2bn	40%
Ergomed	Permira Funds	£700m	+10%
Yourgene	Novocyt (NCYT)	£17m	+74%

**Based on consideration rather than share price movement*
Source: LSE, Refinitiv, Hardman & Co Life Sciences Research

Having peaked in August 2021 on the back of COVID-19-related benefits, particularly vaccines and diagnostics, the NASDAQ Biotech Index (NBI) began to correct. At that point in time, valuations were considered particularly high, as evidenced by a relatively low level of M&A activity in the sector and companies likely demand for more capital. This also coincided with investors becoming more risk-averse, due to the general global economic outlook. Following a significant correction in 2022, the NBI rose 4.1% in 2023, despite the continuing underperformance of Moderna (MRNA), which heavily influences the index. Therefore, our index of UK healthcare stocks fared poorly relative to their US peers.

Performance of Hardman Healthcare Index vs. NASDAQ Biotech rebased



Source: Refinitiv, Hardman & Co Life Sciences Research

In our opinion, the main reason for this is two-fold. First, market awareness of the need for more capital in some companies has resulted in the "mark down/sell-off/shorting" of a number of stocks in the index. Secondly, the consequence of the lack of capital has meant that insufficient progress has been made with the development and commercialisation of novel healthcare technologies over the past year against market expectations.

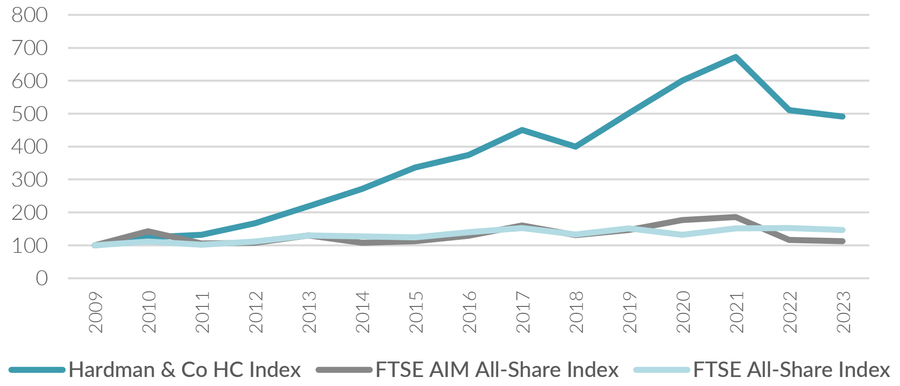
Although the HHI underperformed the NBI (peers) and the broader-based FTSE All-Share Index, it did still outperform the FTSE AIM All-Share Index. Since inception, the HHI has seen a CAGR of 12.0%, compared with 3.3% for the FTSE All-Share Index and 0.5% for the FTSE AIM All-Share Index, highlighting the attractiveness of the sector as a long-term investment.

Comparison of Hardman Healthcare Index with London markets, 2009-23

@ 31 Dec	2009	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	CAGR
	Index	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	Δ	%
Hardman & Co Healthcare Index	**98.4**	31.2%	24.1%	23.9%	9.7%	20.3%	-10.0%	25.3%	19.9%	12.0%	-24.1%	-3.7%	**12.0%**
FTSE AIM All-Share Index	**654.2**	20.3%	-17.5%	5.2%	14.3%	24.3%	-18.2%	11.6%	20.7%	5.2%	-31.7%	-8.2%	**0.5%**
FTSE All-Share Index	**2772.0**	16.7%	-2.1%	-2.5%	12.5%	9.0%	-13.0%	14.2%	-12.5%	14.5%	-3.2%	3.8%	**3.3%**

Source: London Stock Exchange, Hardman & Co Life Sciences Research

Performance of Hardman Healthcare Index – rebased



Source: London Stock Exchange, Hardman & Co Life Sciences Research

Comparison with the majors

All UK healthcare majors underperformed in 2023

In order to put the share price movement of our – generally – small market capitalisation index constituent companies into perspective, the following table shows the performance of the three major UK healthcare companies over the same period. Despite the traditionally defensive nature of healthcare, the UK majors failed to benefit from the difficult global economic environment, with all three underperforming the main index.

Performance of healthcare majors, 2022-23

Company	Ticker	Share price (p) 31 Dec 2022	Share price (p) 31 Dec 2023	Change 2023	CAGR 2013-23
AstraZeneca	AZN	11,218	10,600	-5.5%	11.5%
GSK	GSK	1,438	1,450	0.8%	-1.1%
Smith & Nephew	SN.	1,110	1,078	-2.9%	2.3%

Source: Hardman & Co Life Sciences Research

Despite generating a fairly regular flow of news, AstraZeneca (AZN) underperformed the UK index for the first time in several years. It had some disappointments in its R&D pipeline and some of its more recently launched drugs have not seen the expected growth rates given their strong early commercial uptake seen in 2022.

The demerger of Haleon has had little benefit on a more-focused GSK. Just after the demerger, the company was hit by the filing of litigation in the US claiming a causal association between ranitidine (Zantac) therapy and the development of cancer. In our opinion, there was little to support these claims, especially given the successful patient outcomes after billions of uses of the drug since launch. In 2023, GSK made a modest out-of-court settlement, but this did not trigger a re-rating back to the level seen prior to the claims first being made. At the end of the year, management indicated that it was going to embark on significant M&A activity in 2024, but this is expected to be in the form of licensing in drugs, rather than company takeovers, because of its current level of indebtedness. It will be interesting to see what the company does (see 2023 M&A on next page).

Smith & Nephew (SN.) has, generally, been a weak performer in 2023. Although there was an uplift in the shares following the reporting of 2022 results, the stock faced corrections after reporting 1Q'23 and 1H'23 results, since when there has been a modest recovery. I am surprised that the perennial (every year for >30 years!!) acquisition rumours did not re-ignite when it hit its low point in October.

Resurgence in M&A activity in 2022…

…followed by another 35 deals in 2023 worth a staggering $137.9bn…

Big M&A deals in 2023

The significant devaluation of biotech companies between August 2021 and July 2022 acted as a catalyst for major pharma to pick up suitable opportunities to boost their pipelines and commercial offerings. In 2022, 33 deals were announced, with a total consideration of $83.7bn. This has been followed in 2023 with a further 35 deals for a staggering $137.9bn. The largest of these deals are shown in the following table. Readers should note that these figures do not include a number of acquisitions of small, private companies, where information in the public domain is extremely limited.

Major biotech M&A in 2023 – top 15 deals

Date	Target	Acquiror	Consideration ($bn)
Mar-23	Seagen	Pfizer	43.0
Dec-23	Karuna Therapeutics	Bristol Myers Squibb	14.0
Apr-23	Prometheus Biosciences	Merck	10.8
Nov-23	ImmunoGen	AbbVie	10.1
Dec-23	Cerevel Therapeutics	AbbVie	8.7
Jul-23	Reata Pharmaceuticals	Biogen	7.3
Apr-23	Iveric Bio	Astellas Pharma	5.9
Oct-23	Mirati Therapeutics	Bristol Myers Squibb	4.8
Dec-23	RayzeBio	Bristol Myers Squibb	4.1
Jun-23	Chinook Therapeutics	Novartis	3.2
Mar-23	Provention Bio	Sanofi	2.9
Dec-23	Carmot Therapeutics	Roche	2.7
Jun-23	DICE Therapeutics	Eli Lilly	2.4
Apr-23	Bellus Health	GSK	2.0
Jul-23	Versanis	Eli Lilly	1.9
35 deals			**$137.9bn**

Source: Hardman & Co Life Sciences Research

Reasons for continuing M&A activity

- Major pharma companies, in general, have strong balance sheets, with many having built up large cash piles during the pandemic.
- Revaluation of biotechs has made processes more reasonable, and forced target management teams to reconsider fair value.
- The advent of drugs with mega sales (>$10bn p.a.) has increased exposure to patent expiry, with the next patent cliff towards the end of decade.
- Internal R&D is not generating a sufficient number of new drugs to sustain growth and overcome the pending patent cliff. However, there was a bounce back in the number of FDA approvals in 2023 to 56 versus 37 in 2022.

46% of deals by seven companies

Seven companies accounted for most deals

Deals were led by the major pharmaceutical companies. In 2023, 46% of all deals were announced by just seven companies, representing 79% of the total consideration.

Major pharma M&A activity – 2023

Acquiror	Ticker	# deals	Total consideration ($m)
Pfizer	PFE	1	43,000
Bristol Myers Squibb	BMY	3	22,900
AbbVie	ABBV	2	18,800
Merck & Co	MRK	1	10,800
Eli Lilly	LLY	4	5,760
Novartis	NVS	2	3,700
AstraZeneca	AZN	3	3,338

Source: Hardman & Co Life Sciences Research

Changes to HHI composition

As highlighted earlier, following on from 2022, 2023 was characterised by a number of trade sales. This necessitated some alterations in the company composition of our index. The deletions and additions are shown in the following table. (Please note that the additions come in immediately, whereas the timing of closing a deal might affect when it is fully eliminated from the index.)

Changes to HHI composition

Deletions	Additions
Biodexa (ex-Midatech)	BenevoletAI
Caretech	Creo Medical
Diurnal	Immunocore
Emis Group	
Ergomed	
Yourgene	

Source: Hardman & Co Life Sciences Research

To keep the balance and broad spectrum of healthcare technologies that are covered by the index, Emis Group has been replaced by Immunocore, the Oxford-based NASDAQ-listed immunology company. Benevolent AI has been introduced so that the index has exposure to the trendy artificial intelligence (AI). Although Yourgene has been removed from the index in its own right, it is still, of course, effectively included in the index, having been taken over by Novacyt.

Next year, we will face quite a problem, having to replace the £4.5bn contribution from Abcam following its acquisition by Danaher.

Movers and shakers

Of the 52 companies included in the HHI, only 15 saw an increase in their share prices during 2023; one company was flat and the remaining 36 decreased.

17 companies outperformed and 35 underperformed

Compared with the movement in the index, 17 companies outperformed and 35 underperformed.

Given the large portfolio of constituent companies, we usually focus on both the top five (outperformers) and the bottom five (underperformers), and we try to offer a short explanation as to why the shares performed in the way that they did.

Best and worst performers in 2023 (share price rises and falls)

------------------ Top five	------------------			----------------- Bottom five	-----------------		
Rank	Company	Ticker	Δ	Rank	Company	Ticker	Δ
1	hVIVO	HVO	138%	48	Redx Pharma	REDX	-66%
2	NIOX Group	NIOX	84%	49	BenevolentAI	BAI	-69%
3	Creo Medical	CREO	82%	50	Angle	AGL	-77%
4	Abcam	ABCM	54%	51	Deltex Medical	DEMG	-85%
5	Destiny Pharma	DEST	31%	52	Advanced Oncotherapy	AVO	-86%

Source: Hardman & Co Life Sciences Research

The "top five"

hVIVO (HVO)

Customers increasingly confident HVO will deliver contracts in timely manner

HVO has always had considerable promise, being the only company in the world with a specialist human challenge testing facility for use in the clinical development of vaccines and anti-viral drugs. The company has developed a strong portfolio of human challenge study models for a number of conditions, including influenza, COVID-19, respiratory syncytial virus (RSV), human rhinovirus, asthma, malaria and cough. Potential customers have increased confidence that HVO can deliver on contracts in a timely manner, having opened a new and enlarged human testing facility in 2022. This has resulted in a regular flow of new contracts from major pharmaceutical and biotech companies in 2023, which should be reflected in good financial results for 2023, and even stronger outcomes likely in 2024 and 2025. The market quickly responded to the contract news, with the shares rising 138% over the year. Another new contract earlier this month means that 2024 has also got off to a good start.

NIOX Group (NIOX)

Focused NIOX is profitable and cash-generative…

…and now paying dividends

NIOX has evolved from the old Circassia group, which was a disastrous investment. Today, NIOX is focused on improving asthma diagnosis through its fractional exhaled nitric oxide (FeNO) test, which is a by-product of inflammation found in the air that you breathe out. Sales are made through distributors and are strong in countries where air pollution is a problem, such as the US and China. The business is profitable, growing, and cash-generative. In 2023, NIOX paid its first dividend (2.5p special dividend) and expects to pay a final dividend for fiscal 2023, due to be announced in March 2024. Consequently, the shares have seen a good recovery in 2023, rising 84%.

Creo Medical (CREO)

Speedboat really starting to get sales traction

In 2022, CREO progressed its "Build, Buy and Partner" strategy. The "Build" part was exemplified by increasing sales traction for its "Speedboat® Inject" (electrosurgical device); whereas partnerships were enhanced through significant deals with major robotics companies, Intuitive and CMR. Although the market started to sit up and take note, it was also aware that, to really move forward, the company needed to strengthen its balance sheet. Consequently, when CREO raised £33.7m (gross) in February 2023, the Placing, Subscription and Open offer was significantly over-subscribed and the stock responded positively. Despite a reasonably regular flow of news, in particular the accelerated development and FDA approval of Speedboat UltraSlim (October) and a capital markets day (7 November), the shares traded in a fairly tight range until December. Then announcements that Speedboat UltraSlim had been used already in both Europe and the US rekindled interest in the company and the shares finished at a year-high of 46p (+82%).

Abcam (ABCM)

Bought by Danaher for $5.7bn/£4.5bn in 4Q'23

Abcam was a unique company, established to fulfil a gap in the market for tools to help researchers in the identification and discovery of antibodies. It evolved from a small Cambridge-based operation, selling its products to thousands of customers all over the world. However, it appeared to have reached a peak in its growth strategy. Following a strategic review, the board decided to put itself up for sale. Danaher won the bidding with a cash offer of $24.0 per share, valuing the company at $5.7bn/£4.5bn.

While it was very profitable, growth was lumpy due to the need to reinvest operating profit back into R&D to develop the next generation of products. The problem for potential investors was that Abcam always appeared to be relatively expensive, but its uniqueness and reinvestment strategy meant that it would always be expensive. However, those that did take the plunge have done very well, with a CAGR of 16.4% in its market capitalisation over the past 10 years, all in the absence of any capital increases, apart from when it listed on NASDAQ. It will be interesting to see what Danaher can achieve with the company, putting its greater financial resources behind it.

Destiny Pharma (DEST)

Signed two important co-development deals…

…but needed more capital

2023 was a year of recovery for DEST, albeit its good performance (+31% to 70p) still leaves it well off its 2021 peak. In February, the company signed an important US co-development and commercialisation deal for NTCD-M3 (prevention of *Clostridioides difficile* (*C.diff*) infection) with Sebela Pharma, a small private pharma specialising in women's health and gastroenterology. However, the market ignored the headline long-term potential figure of $570m, preferring instead to focus on the miniscule ($1m) upfront payment, which was insufficient to avoid a capital increase to strengthen the balance sheet. This duly arrived a few days later at a 40% discount to the close immediately before the Sebela deal. Confidence was also dented by the paltry (£25k) support for the fundraise by the well-paid executives on the board. DEST then parted company with its CEO in May. The first signs of recovery came in July with the appointment of a new CEO (Chris Tovey), followed by publication of XF-73 (antibiotic) data in October. The stock ended the year about 10p off its peak. The only item of significance in its year-end update (4 Jan 2024) was that, based on its current business plan, the company has sufficient cash until 1Q'25.

The "bottom five"

*Advanced Oncotherapy (AVO)**

Market was shocked by the size of investment needed to finish LIGHT project

At the start of 2023, everything looked positive for AVO provided that it could raise the necessary funds to complete its highly technical project – a proton beam therapy for the treatment of cancer. The company had completed the major scientific milestone of proving that it could accelerate a proton beam to the highest energy level required for treatment – 230MeV. 2023 was seen as the year that it would complete the project and start first patient treatments. However, all of this was predicated on the assumption that it would be able to raise the necessary capital.

When the company announced that it would need £70-£80m over two years, the market took fright and the share price collapsed. This made it even more difficult to raise capital without wiping out existing shareholders. The shares were suspended in July because the company was unable to publish its 2022 accounts, and this will remain the case until its funding requirement is resolved. In October 2023 and reiterated in January 2024, the company released a statement indicating that a non-binding term sheet had been signed with a potential investor for $80m. As part of any financial restructuring, much of its current debt would be converted into equity. Having followed this project from the very beginning, I do hope that AVO can get LIGHT to a conclusion, because there is little doubt about the pent-up global demand for such a machine.

Deltex Medical (DEMG)

DEMG has been disastrous investment

An investment in DEMG has been disastrous, with the share price declining 99% over the past 10 years. Although there is a reasonable rationale for its haemodynamic monitoring technology, it is a case of too little (advantages), too late (development very protracted). Various management teams have all struggled to generate sales traction of its TrueVue system. I also recall, a few years ago, that the company organised a practical demonstration for analysts – and the nurse could not get the product to work, so we all went home disappointed!! Nothing has happened since to change my view. DEMG is operating in a competitive market that has moved on from its technology.

Angle (AGL)

Great technology…

…but difficult to get traction against major competitors

AGL does have an impressive liquid biopsy technology (Parsortix®), which is highly sensitive and accurate in the measurement of circulating tumour cells. However, it has taken a long time to get to the commercialisation-stage that it has reached today and investment by major diagnostic companies has seen competing technologies moving apace – notably Grail's all-encompassing early cancer screening test. AGL started 2023 badly, with a negative trading update and restructuring announcement on the first day back after the New Year holiday. There was a bounce in April when it announced a services contract (Crescendo Biologics) and partnership agreement (BioView). A further bounce was seen in September following an update to the market with its interim results, but much of this had been reversed by November when the company issued a trading update and further restructuring to preserve cash. Although the sales growth rates read impressively (+120% for 2023), it is off an incredibly small base and is insignificant (£2m) in absolute terms compared with the massive market opportunity ($bns). The announcement also stated that the company has sufficient cash until 2Q'25. Extrapolating this back, AGL will need to publish its 2023 results around the end of 1Q'24 in order to get auditor sign-off for its 12 months' working capital requirements. Also, in our opinion, the market should expect another equity raise prior to the announcement of its interim results in September 2024.

Benevolent AI (BAI)

Grossly overvalued when it reversed into SPAC…

BAI is a European-based artificial intelligence (AI) company, with drug discovery and research capability that can take a drug through the entire development process, from discovery to late-stage clinical development. Originally a private company, BAI was effectively valued when it reversed into a SPAC (Odyssey) quoted on the Amsterdam stock exchange in April 2022. At that point in time, the business combination was valued at €1.1bn/£955m pre-money and €1.4bn/£1.22bn with the €255m/£220m raised. As seen with many examples in the US, companies are seriously overvalued when they reverse into SPACs, with the consequence that the shares tumble when the true valuation is afforded by the market. BAI was no different. On listing, the company had one drug in early clinical trials for atopic dermatitis, two putative drugs in pre-clinical development, two licensing deals and a host of interesting ideas, however, compared with other companies around the same size and stage of development, its valuation was excessive.

...and now needs more cash

For the first 18 months since listing, the valuation has not been particularly important, because the company was sitting on a very large cash pile. However, this business is seriously cash-negative, it employs a lot of people, and is burning in excess of £80m p.a.; so, at the end of December 2023, we estimate that the gross cash is down to ca.£45m, which is insufficient to get auditor sign-off of its 2023 accounts regarding working capital requirements. Consequently, since listing, the shares have lost 88% of their value. Its precarious position is compounded by the fact that the CEO abruptly left the company in September 2022 and a new CFO has been appointed, whose first task will be to tap the markets for more cash.

Redx Pharma (REDX)

REDX plans completely scuppered

2023 has been a poor year for REDX, with its strategic plans scuppered at the last minute, consequently, the share price had been in a downward trend all year, finishing down 66% at 22p. In February, REDX announced a business combination with Jounce Therapeutics (JNCE), a cash-rich ($155m) NASDAQ-listed biotech company, which has seen clinical trial failures. This would have seen REDX move its listing to NASDAQ, provide it with a few years of working capital, and potentially realise a greater valuation. However, while all the legal and regulatory work was being undertaken, Jounce received an alternative cash offer from Concentra in March, which was unanimously approved by its board, so it and withdrew from the REDX deal. This left REDX in limbo, and with a high cash burn (£30-£35m p.a.), the need to raise more capital. This duly arrived in October at 26p per share, but the gross new funds (£14.1m) only extend the cash runway from 1Q'24 to 3Q'24, so investors should be aware that another cash call is likely ahead of its interim results – usually released in May.

Ongoing need for more capital

Investors are well aware that the healthcare industry, particularly for small companies with products in development or the early stages of commercialisation, is capital-intensive. Most institutional investors that commit to this sector are buying into a new technology and know that they must be in it and supportive for the long term. Consequently, it should come as no surprise that 15 (29%) companies in our index took the opportunity to raise £229m in 2023 to support their operational activities. It is not the purpose of this document to comment on every company; however, we would like to point out some concerning trends.

Deep discounts

The range of discounts offered to obtain support for an equity raise ranged from a premium of 27% (Oxford Nanopore) to 99% (Yourgene). A worrying trend was the number of companies (four – Allergy Therapeutics, Deltex Medical, Genedrive, and Yourgene) that needed deeply discounted offerings in order to obtain a successful outcome, which, given that pre-emption rights have been voted away, means that existing shareholders are effectively wiped out.

Yourgene

Takeout price looks good compared with fund raise…

…but many shareholders forced to crystalise losses

Deep discounts were first seen at the end of 2022 when the board of Yourgene raised £6.4m of gross new capital (£5.9m net) at 0.3p per share – a 94% discount to the six-month average closing share price – effectively wiping out existing shareholders. Although there was a retail offer, it is restricted to a few trading platforms, which were inaccessible to many existing shareholders. Having said that, they might have considered this to be a lucky break as the shares continued to drift in 1Q'23 down to 0.19p. In early July, shareholders were put out of their misery with a 0.5p cash offer from Novocyt. Although this appears to be a healthy premium compared with the fund raise, it forced many long-term shareholders to crystalise significant losses.

Allergy Therapeutics

Two shareholders could end up with 98.5% of company

A similar decision was made by the board of AGY. Although the company had good shareholder support, new working capital and funds to finish off its clinical trials came at a price. Its two major shareholders underwrote a £40m raise, but this was at 1p per share when the shares were trading around 6.25p per share. However, in this case, existing shareholders were given the opportunity to participate on the same basis – six shares for every one held at 1p per share – which was a 'no-brainer' given that the shares had been trading at an ex-rights price in the range 1.5-1.7 for some time before the decision needed to be made. Despite this, SkyGem Acquisition Ltd/ZQ Capital (65%) and Southern Fox (27.4%) now hold 92.4% between them and they are also providing loan facilities to cover its current working capital requirements. This, too, comes at a cost, with up to 1,000,000,000 warrants being issued in addition to the 12% coupon. In the event that these warrants are exercised in full, these two shareholders would control 98.5% of AGY. The shares are currently suspended because AGY was unable to publish its annual report within six months of the period-end due its auditor (BDO LLP) "…*requiring additional time to complete its audit…due to resource availability within the audit engagement team…*". Hmmm!!

Genedrive

Avoid when its too complicated to get your head around

As the old saying goes: "*if it is difficult to understand, it is almost certainly detrimental to shareholders*". Never has this been more true than in the case of Genedrive (and more recently, Sareum). Although I accept that the board was probably in a difficult position with a shareholder list of mostly retail investors, but desperate for cash, the loan facility announced in March 2023 with Riverfort Global Opportunities PCC Ltd (Riverfort) is extremely complex. After more than 35 years as an analyst, I consider myself reasonably financially literate. However, I can honestly say that I have read this agreement at least 10 times and I still do not fully understand it!

In summary, Riverfort made £5m available to the company. £2m was drawn down immediately with the remaining £3m available for £0.3m monthly drawdown subject to certain conditions being fulfilled. The loan capital is being repaid through the issuance of new shares to Riverfort priced on a specific calculation (reference price) and can be sold in the market, based on a series of conditions related to daily volumes traded. On each drawdown, Riverfort also receives warrants equal to 40% of the drawdown at the recalculated reference price, exercisable at 140% of this reference price. The following table shows what has happened to date.

Summary of cost of Riverfort loan facility

Date	Drawdown (£m)	Shares	Warrants	Reference price(p)	Exercise price (p)	Potential raise (£m)
31-Mar	2.0	6,500,000	2,500,000	32.0	44.8	1.12
02-Jun	0.3		682,730	17.6	24.6	0.17
05-Jul	0.3		724,997	16.6	23.2	0.17
04-Aug		3,050,000				
21-Sep		3,100,000				
20-Oct		3,240,000				
29-Nov	0.3	3,300,000	1,614,669	7.4	10.4	0.17
06-Dec		3,400,000				
07-Dec		3,650,000				
20-Dec		3,650,000				
02-Jan	0.6		3,093,915	7.8	10.9	0.34
10-Jan		3,750,000				
Total to date	**3.5**	**33,640,000**	**8,616,311**			**1.96**
% dilution		36.4%				

Source: Hardman & Co Life Sciences Research

In my opinion, this deal is very bad for shareholders. To date, the issue of shares to repay the loan capital represents dilution of 32.3%. The main reason for this is that Riverfort is not a long-term shareholder, as evidenced by the fact that it sold down its holding of 6.5m shares received in April to only 2.95m (-55%) by July. Even though it has received more shares, its holding is not disclosed as being >3.0% declarable threshold. Therefore, it is continually selling shares, which, in turn, causes the share price to fall, making the next drawdown even more expensive.

Based on the current share price, Genedrive will need to issue an estimated18.25m more shares and a further 8.0m warrants, which would provide the potential to raise another £0.85m. The total issue of shares will represent dilution of 56% and in the event that all the warrants are exercised, this would increase to 78%, but potentially raise a further ca.£2.8m. However, given that most of the warrants are out of the money, there is a high probability that the warrants will not be exercised.

Amazingly, Sareum announced a similar deal with the same investor in November. On the evidence of GDR, guess where the share price is going!

Potential capital raises in 2024

Although by no means comprehensive, a quick assessment of the latest balance sheets and statements from companies in our index suggests that there will a number of cash calls in 2024. Some of these will occur imminently in order to get auditor sign-off of 2023 accounts for the 12 months' working capital need, whereas others will be later in the year ready for sign-off of 2024 accounts.

Our assessment is relatively simple, looking at the latest stated, or estimated current, cash position and annualisation of the monthly cash burn rate. No consideration has been made for any licensing deals, milestones or other deals for products or services which these companies could sign.

The following table provides a list of companies in our healthcare index known to require, or likely to need, a cash injection during 2024.

Companies in HHI likely to require a cash injection during 2024

Company	Ticker	*Gross cash (£m)	*Annual burn (£m)	Comment
Advanced Oncotherapy	AVO	0.1	-2.4	Term sheet with potential investor
Allergy Therapeutics	AGY	19.1	-28.0	"Cash runway to end-January"
Angle	AGL	15.0	-12.0	Cash runway to 2Q'25
Avacta	AVCT	26.0	-17.0	Currently using convertible loan
Benevolent AI	BAI	45.0	-70.0	Needs cash for auditor sign-off
Destiny	DEST	7.4	-6.0	"Funded to 1Q'25"
e-Therapeutics	ETX	24.8	-16.5	Will need cash for auditor sign-off
Futura Medical	FUM	9.4	-9.5	Needs cash for auditor sign-off
Genedrive	GDR	0.8	-4.0	Only 5 more monthly drawdowns
ImmuPharma	IMM	1.0	-1.2	Burn offset by R&D tax & Lanstead
Redx	REDX	23.5	-32.0	"Cash runway into 3Q'24"
ReNeuron	RENE	5.1	9.5	"Cash injection by start of 2Q'24"
Synairgen	SNG	12.0	-15.0	"activities until at least end 3Q'24"
ValiRx	VAL	1.6	2.4	Will need cash before year-end

**Latest company announcement and/or Hardman & Co estimate for 31 December 2023*
Source: Hardman & Co Life Sciences Research

I hope that you have enjoyed this opinionated review of UK healthcare in 2023 and wish you the best of luck with stock selections in 2024!

About the author

Dr Martin Hall

Martin's career in the City started as a healthcare analyst in 1987, working at Morgan Grenfell and then UBS. He joined HSBC in 1992, where he became Head of Global Pharmaceutical/Healthcare Equity Research. In 2005, he set up as an independent Life Sciences Analyst and Corporate Broker under the umbrella of Eden Financial Limited. Martin is acknowledged for his thought-provoking and opinionated research. He joined Hardman & Co in June 2013.

Martin qualified as a pharmacist (B.Pharm.Hons) at the School of Pharmacy, University of London, and has a PhD in Neuropharmacology, also from the University of London. After two years of post-doctoral research under a Royal Society Fellowship at the Collège de France, Paris, he became leader in Biochemical Pharmacology at the Parke-Davis Research Centre in Cambridge. Martin is a member of the Royal Pharmaceutical Society of Great Britain.

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The full detail is on page 26 of the full directive, which can be accessed here: http://ec.europa.eu/finance/docs/level-2-measures/mifid-delegated-regulation-2016-2031.pdf

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