Bellevue Healthcare Trust

MAY 2023

Factsheet

Marketing document

Investment focus

Bellevue Healthcare Trust intends to invest in a concentrated portfolio of listed or quoted equities in the global healthcare industry. The investable universe for the fund is the global healthcare industry including companies within industries such as pharmaceuticals, biotechnology, medical devices and equipment, healthcare insurers and facility operators, information technology (where the product or service supports, supplies or services the delivery of healthcare), drug retail, consumer healthcare and distribution. There are no restrictions on the constituents of the funds portfolio by index benchmark, geography, market capitalisation or healthcare industry sub-sector. Bellevue Healthcare Trust will not seek to replicate the benchmark index in constructing its portfolio. The fund takes ESG factors into consideration while implementing the aforementioned investment objectives.

Fund facts

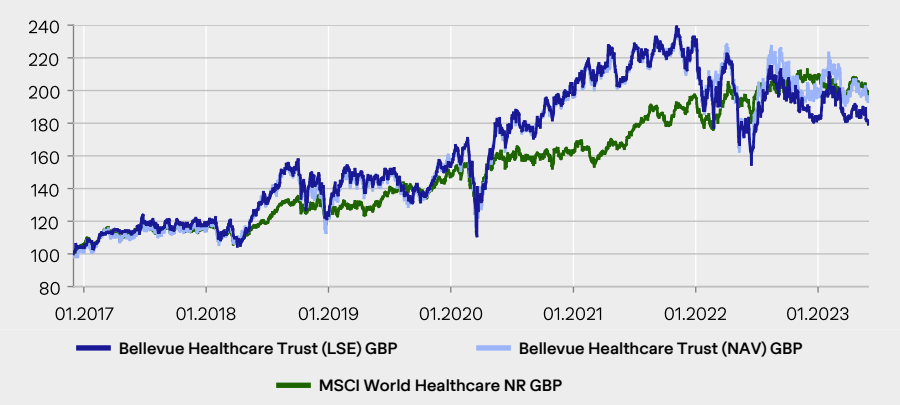
Share price	147.40
Net Asset Value (NAV)	159.62
Market capitalisation	GBP 809.11 mn
Investment manager	Bellevue Asset Management (UK) Ltd.
Administrator	Apex Listed Companies Services (UK) Ltd.
Launch date	01.12.2016
Fiscal year end	Nov 30
Benchmark (BM)	MSCI World Healthcare NR
ISIN code	GB00BZCNLL95
Bloomberg	BBH LN Equity
Number of ordinary shares	548,924,670
Management fee	0.95%
Performance fee	none
Min. investment	n.a.
Legal entity	UK Investment Trust (plc)
EU SFDR 2019/2088	Article 8

Key figures

Beta	1.37
Correlation	0.70
Volatility	28.3%
Tracking Error	20.82
Active Share	91.14
Sharpe Ratio	0.28
Information Ratio	0.02
Jensen's Alpha	-2.21

Source: Bellevue Asset Management, 31.05.2023;
Calculation based on the Net Asset Value (NAV) over the last 3 years to 31 May 2023.

Indexed performance since launch



Cumulative & annualised performance

Cumulative

	1M	YTD	1Y	3Y	5Y	10Y	ITD
Share	-3.2%	-1.8%	-0.1%	2.0%	43.1%	n.a.	79.3%
NAV	-3.2%	-3.2%	10.2%	10.6%	54.1%	n.a.	94.2%
BM	-2.6%	-4.6%	1.6%	21.5%	70.0%	n.a.	98.0%

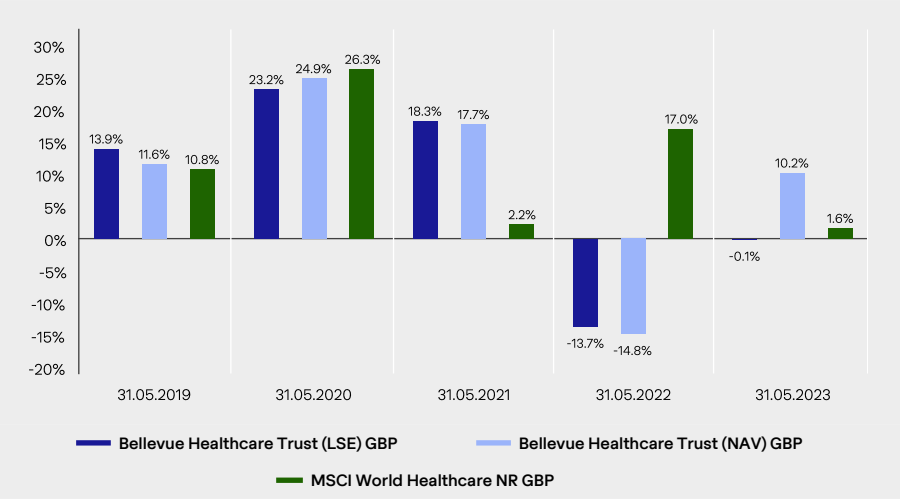
Annualised

1Y	3Y	5Y	10Y	ITD
-0.1%	0.7%	7.4%	n.a.	9.4%
10.2%	3.4%	9.0%	n.a.	10.8%
1.6%	6.7%	11.2%	n.a.	11.1%

Annual performance

	2018	2019	2020	2021	2022	YTD
Share	4.9%	22.7%	29.1%	16.6%	-21.0%	-1.8%
NAV	8.6%	25.9%	25.7%	15.2%	-11.1%	-3.2%
BM	8.8%	18.4%	10.3%	20.8%	5.8%	-4.6%

Rolling 12-month-performance



Source: Bellevue Asset Management, 31.05.2023; all figures in GBP %, total return / BVI-methodology

Past performance is not a reliable indicator of future results and can be misleading. Changes in the rate of exchange may have an adverse effect on prices and incomes. All performance figures reflect the reinvestment of dividends and do not take into account the commissions and costs incurred on the issue and redemption of shares, if any. The reference benchmark is used for performance comparison purposes only (dividend reinvested). No benchmark is directly identical to the fund, thus the performance of a benchmark is not a reliable indicator of future performance of the Bellevue Healthcare Trust to which it is compared. There can be no assurance that a return will be achieved or that a substantial loss of capital will not be incurred.

Welcome to our May missive. The sun is shining at last and the manufactured US debt ceiling crisis is thankfully behind us. One can only hope that quieter and more rational markets are ahead.

And yet, there are still so many external execrations and contemporaneous catastrophes to confute the harried investor. It feels to us that caution remains a watchword and betting all out on a return to robust economic growth is some months away yet.

We remain optimistic that the defensive growth characteristics and attractive relative valuations of innovative healthcare companies will shine through to investors start looking at companies rather than market-level positioning. Where else can you find such compelling quality growth at a reasonable price?

Monthly review

The wider market

During May ongoing macro-economic and interest rate concerns, compounded by the default risks around the US debt ceiling being breached led to a generally negative 'risk-off' mindset. The notable exceptions to this were AI-linked software and semi-conductor stocks, which continued their upward march. Overall, the MSCI World Index declined 1.3% in dollars (+0.3% in sterling).

Energy stocks lagged on continued disappointing macro data from China suggesting a sluggish recovery and thus subdued demand for energy, especially crude oil. This also spilled into the materials sector, despite the increasing focus on the coming crunch in Copper and Lithium that will be necessary in facilitating the clean energy transition.

Sector	Monthly perf
Semiconductors & Semiconductor Equipment	+19.7%
Software & Services	+8.2%
Automobiles & Components	+7.6%
Media & Entertainment	+6.9%
Technology Hardware & Equipment	+4.1%
Consumer Discretionary Distributors	+2.6%
Consumer Durables & Apparel	+0.0%
Commercial & Professional Services	-2.2%
Transportation	-2.4%
Capital Goods	-3.6%
Healthcare Equipment & Services	-4.0%
Financial Services	-4.2%
Consumer Services	-4.2%
Pharmaceuticals, Biotechnology	-4.5%
Equity Real Estate Investment	-5.1%
Banks	-5.2%
Consumer Staples Distribution	-5.7%
Telecommunication Services	-6.2%
Utilities	-6.2%
Food, Beverage & Tobacco	-6.7%
Insurance	-6.7%
Real Estate Management & Development	-6.9%
Materials	-7.5%
Household & Personal Products	-9.7%
Energy	-10.5%

Source: Bellevue Asset Management, 31.05.2023

Investors continue to wrestle with a preponderance of mixed signals regarding the direction of the economy in the US, Europe and China (the outlook for the UK is sadly much clearer and more negative). The number of existential crises that sentiment has had to weather in recent months (war, inflation, energy shortages, increasing debt costs, bank failures, debt ceiling crisis, blips of COVID resurgence) feels unprecedented and wearing for all concerned.

Navigating the markets feels like one of those 'escape room' experiences, with an endless series of challenges that require one to pivot to thinking about a new subject. Even so, the consumer (especially in the US) remains indefatigable and sentiment just won't tip over into outright bearishness. People continue to spend and companies seem still to manage to pass on higher costs, preserving margins.

Broadly speaking, earnings expectations are falling, but this is like watching a feather fall gently to the floor as opposed to a tsunami of profit warnings. Employment just won't decline and the AI frenzy is keeping broad market indices in positive territory compared to the recent lows of October 2022. We are gliding sideways at pace and it is difficult to foresee when the market will re-align to consider company fundamentals ahead of these myriad other factors.

Healthcare

During May, the MSCI World Healthcare Index declined 4.3% in dollars (-2.8% in sterling), underperforming the wider market by 3.0%. The sub-sector performance breakdown is summarised in Figure 2 and suggests a general tilt in favour of the most defensive elements of healthcare (Distributors & Managed Care did well, Dental fared worst and a number of higher growth areas were laggards: Healthcare IT, Healthcare Technology, Tools).

Dental, which is the apotheosis of consumer discretionary was the worst performer, followed by Facilities (hospital operators), whose operating performance is dependent on both employment and the levels of US Government spending for welfare and social security; both were feared targets for the debt ceiling discussions.

The notable outlier to this pattern of caution is Diagnostics, which seemed to hold up well (rather than perform well despite being very much in the high growth, high beta and negative size factor buckets). However, the majority of this relative outperformance can be attributed to Exact Sciences.

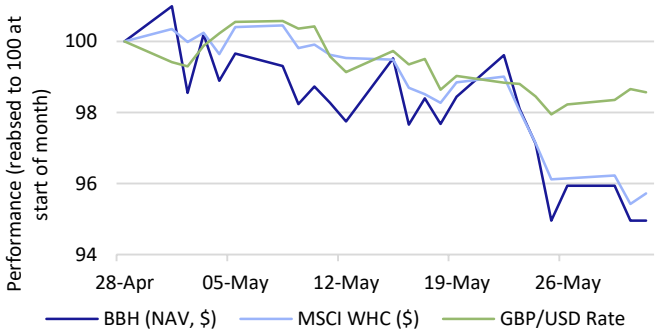
Excluding Exact, the sub-sector would have declined ~3.6% over the month. Its strong performance during May was driven by strong Q1 results and revised FY23 guidance, which still appears very conservative to us.

	Weighting	Perf (USD)	Perf (GBP)
Distributors	1.6%	2.7%	4.3%
Diagnostics	1.5%	-0.3%	1.2%
Managed Care	10.5%	-2.6%	-1.1%
Services	2.2%	-2.6%	-1.1%
Diversified Therapeutics	37.9%	-3.0%	-1.5%
Focused Therapeutics	8.4%	-5.1%	-3.6%
Med-Tech	14.2%	-5.2%	-3.7%
Healthcare Technology	0.9%	-6.7%	-5.3%
Conglomerate	11.1%	-6.9%	-5.5%
Tools	8.0%	-7.1%	-5.5%
Other HC	1.3%	-7.5%	-5.6%
Healthcare IT	0.5%	-7.9%	-6.5%
Generics	0.3%	-8.4%	-7.0%
Dental	0.6%	-8.9%	-7.5%
Facilities	1.1%	-9.1%	-7.7%
Index perf		**-4.3%**	**-2.8%**

Source: Bloomberg/MSCI and Bellevue Asset Management, Weightings as of 28.04.2023, Performance to 31.05.2023

The Trust

During May, the Trust's Net Asset Value declined by 3.2% in sterling to 159.62p, underperforming the total return of the comparator MSCI World Index by 56bp. The evolution of the NAV over the course of the month is illustrated in Figure 3 overleaf:



Source: Bellevue Asset Management, 31.05.2023

Diagnostics (especially Exact Sciences) was the main positive contributor during the month, with Med-Tech the key detractor (notably Axonics). Size factor was again a significant overall influence on the portfolio.

The evolution of the sub-sector weightings is summarised in Figure 4 below and we would make the following comments. We shifted the portfolio onto a more defensive tack in the earlier part of the month (cf. Managed Care) and reduced gross exposure to protect the portfolio around the inevitable debt ceiling market drawdown. We also significantly scaled back our holding in long-standing Top-10 position Sarepta Therapeutics (cf. Focused Therapeutics) into and around the Advisory Committee meeting for its gene therapy product SRP-9001. In the latter part of the month, we deployed additional capital as the debt ceiling debate progressed and this was skewed toward recent laggards in Services and Tools.

	Subsectors end Apr 23	Subsectors end May 23	Change
Dental	1.0%	0.9%	Decreased
Diagnostics	9.5%	11.4%	Increased
Diversified Therapeutics	3.6%	4.0%	Increased
Focused Therapeutics	27.2%	21.3%	Decreased
Healthcare IT	9.2%	8.8%	Decreased
Healthcare Technology	3.9%	3.0%	Decreased
Managed Care	5.5%	7.2%	Increased
Med-Tech	17.4%	18.8%	Increased
Services	14.4%	14.9%	Increased
Tools	8.3%	9.6%	Increased
	100.0%	**100.0%**	

Source: Bellevue Asset Management, 31.05.2023

The investment portfolio is unchanged at 28 companies. Over the month, the leverage ratio fell from 3.6% to 0.9% and we expect this to gradually increase again over the balance of the year. The average discount to NAV declined modestly from 7.4% in April to 6.4% in May and was generally in line with the healthcare investment trust peer group. The share buyback program was active during the month and 0.7m shares were repurchased.

Managers' musings

"The die is cast"

Despite the many and varied challenges facing us all in these troubled times, there finally appears to be a singular, unifying theme at last – the disruptive impact of Artificial Intelligence (A.I., or machine learning). Opprobrium and optimism co-exist in equal measure, with the one consensus view seeming to be that everything is about to change profoundly.

This laser-like focus on AI has been triggered by the public release of Open AI's 'Chat GPT' Large Language Model in November 2022. This was the first opportunity for many private citizens and journalists to play with a powerful Large Language Model (LLM) tool.

For those that have not tried it out, it is a spookily human experience. You submit a query and a few seconds later, it churns out a response, almost as if it is tapping it out on a keyboard. This is a very different experience to searching the internet using Google, where your query instantly provides a series of links to websites whose content bears some resemblance to your enquiry. In general, the more complex the query, the less relevant the suggestions and, regardless, you are going to have to read a fair bit of text to find a clear answer to even a moderately complex question.

On the plus side, the Google approach does allow you to see where the data is being referenced from. We would accord more weight to a paper in Nature or the New England Journal for instance, than to one on a pre-print website.

In contrast, and with a bit of practice on how to submit an enquiry, one can conjure up quite lengthy and natural-sounding responses from Chat GPT; you can even ask it for a reply "in the style of…". Indeed, its creators encouraged this approach during the 'training phase' (this is known as reinforcement learning, where humans rate the responses given and this feeds back into the algorithm).

LLMs and the maths behind so-called Generative AI is not particularly new. The earliest generative AIs were chatbots that we are surely all familiar with on consumer websites and these came to the fore in the early 2000s. The 'LLM' models first appeared in 2018 and are getting better at seeming 'naturalistic' through feedback on responses given, huge advances in processing power and larger training data sets. Some have estimated that the energy bill for the training phase of GPT4 was >$100 million alone.

Eerily naturalistic they may be, but to describe them as an "intelligence" seems a little far-fetched to us; it is still a 'prompt and response' model. However, LLMs do seem to display emergent properties (having knowledge of or understanding of things they have not been specifically trained upon).

The flip-side of these emergent properties is also the ability to mis-understand things or simply make up things that sit outside the training dataset (including false references as to the sources of the "imagined" data). These nonsense answers are endearingly referred to as "hallucinations" by AI boosters. Perhaps a better description of the technology is not "artificial intelligence", but rather a tool that is "just about smart enough to be useful, despite the flaws" (not our own words, but from Vox magazine).

Were one foolish enough to submit such hallucinogenic content to a university tutor as an essay, their description would probably suggest bovines and excrement rather than an extra-sensory experience. LLMs are heuristic tools and are simply trying to figure out the next most logical word in response to the given prompt based on the training dataset, albeit using some fiendishly complex multi-dimensional maths.

For those of us old enough to remember life before and after the debut of Google Search (it launched in 1998, so the under 35s are probably unaware of this world), this current 'revolution' does not feel all that amazing in comparison. That said, the internet and connected technology is now ubiquitous, whereas it was all dial-up, air-gapped internet terminals back then. Moreover, the generalised internet (the 'world wide web') contained nothing very useful at that stage and the world remained an analogue one.

"Upset by an unexpected turn of events"

Moving beyond media (and sell-side) fodder, how is AI going to change our world and, in particular for healthcare, and how revolutionary are

these changes going to be? One of the challenges in foreseeing how models such as Chat GPT 3 & 4 could impact the corporate world is the general nature of their training dataset.

For now, the investor's simplistic answer to this question is to ignore the prospective goldmines and buy the picks and shovels instead. The shovel of AI is the GPU chipset and the share price of GPU market-leader NVIDIA (+129% since the chat GPT launch to c.$1 trillion and +180% over the six months to May 2023) attests to this. Machiavelli would be proud that his axioms regarding historical repetition holds true almost 600 years on. Those inclined to study history further (no need to go back to 17th Century Holland; 1999-2001 will suffice) will also recall how these sorts of things tend to end.

In a world of finite resources, the current speculation on semi-conductor, IT and software companies must be funded from somewhere and it does feel very reminiscent of the late 1990s 'old economy versus new economy' debate ("sell bricks to buy clicks"). Stale old healthcare has been an obvious victim of this trend; the MSCI World Healthcare Index has under-performed the broader MSCI World Index materially since the end of October 2022 (delivering a total US dollar return of +4.0% to the end of May, versus +14.0% for the MSCI World Index).

We estimate that the semi-conductor sector accounted for ~30% of the total return during this period. Within this, NVIDIA was around half that sector's total return. Alphabet (parent of Google, also active in AI), Meta (Facebook, WhatsApp and Instagram and similarly active in AI and Microsoft (Chat GPT's biggest customer and investor) accounted for a further c.40% of the Index's total return.

In our humble opinion, this is truly incredible even compared to the Millenial madness; AI plays drove around three quarters of the total return over the past six months and, within this, the vast majority came from FOUR stocks.

However, the same phenomenon can actually be found within healthcare as well; almost the entire six month total return of the MSCI World Healthcare Index over the same six months can be attributed to the GLP-1 obesity plays Eli Lilly and Novo Nordisk. Well done to anyone who happened to be overweight any of these AI or obesity companies; we will buy you a tulip.

Let us acknowledge once more Graham's axiom that markets are voting rather than weighing machines and come back to the broader question of assessing the impact on the wider (i.e. real) economy. If one submits an enquiry to Chat GPT on a specific topic about which one is already knowledgeable, the answers will seem less than impressive.

This is surely because most of the really interesting data in the world is safely locked away on corporate intranets or in textbooks and journals not freely readable online and thus not in its training data set. It is therefore difficult to extrapolate what this clearly powerful tool might empower if it were let loose on FitBit or Apple's health data or even that of United Healthcare. What could such a 'Generative AI' learn from, say Roche's R&D intranet or Charles River's extensive pre-clinical toxicology repertoire?

"Experience is the teacher of all things"

We won't know the answer to the critical questions posed above until we see them, but there are some instructive examples already regarding the deployment of machine learning that we can illustrate (and also some less compelling stories).

If there is a general rule that we have noted at this point in the "AI cycle", it is that these tools lend themselves to the specific task rather than to generalised insights. They can find patterns but cannot "connect the dots" to infer what the patterns mean in a reliable way (cf. the 'hallucinations') - the human brain isn't obsolete just yet.

Below we list some general examples of situations where we can see AI having a material, positive impact:

- **Medical imaging:** if you are thinking of re-training for a new career, we are not sure that radiographer would be the wisest of choices. The interpretation of scans is very much an art, as anyone who has looked at their MRI or CT scans with their physician in a consultation will attest (even if we don't let on they are often impenetrable to the lay-person).

  However, this sort of pattern recognition is exactly the sort of thing that machine learning can excel at – image data files and suspected diagnosis as an input and hard outcomes data as an output; training the data on scans where the diagnosis has been confirmed as positive or negative in respect of whatever it might be looking for.

  Moreover, this processing can be done almost in real-time. Leaving aside the potential for enhanced accuracy and lower costs, the opportunity to be able to send cancer patients returning for recurrence screening an email in a matter of minutes confirming they are 'all clear' has societal benefits in reducing anxiety for them and their loved ones.

  For those scans where the computer is unsure, it can flag it up to the (few) remaining radiographers for adjudication. The logical denouement is for such capabilities to be built into imaging software supplied with such machines. This will not ultimately be limited to big ticket items; expect the retinal and other scans routinely undertaken by your optician and dentist to go down the same route.

- **Surgical planning and VR visualisation:** it is increasingly the case that minimally invasive surgical tools and robotic assistance are swelling the number of options available to a surgeon in order to address a particular ailment. Even with something as simple as a hernia operation, laparoscopic and robotic approaches offer multiple entry and visualisation routes for different lesion types.

  Surgeon experience comes to the fore in these situations; they will have a good idea which way to go. For a more complex surgery though, particularly one where the outcome may have long-term implications for quality of life, the stakes are higher and a lot of planning takes place ahead of time and there are many variables to take into account.

  We see this as another situation where AI-based software tools can come to the fore. Historical cases and the related scans and baseline parameters are all robust inputs and longer-term outcomes and in-surgery complications are known, making for a useful training set.

  Concentration is critical during surgery, and distractions need to be minimised. At the same time, the surgeon will need key information at critical points. Over time, machine learning can become familiar with what is needed when and present it in an augmented reality (where some data is super-imposed onto a real-time image).

  We have already seen these sorts of tools in the marketplace and we expect them to become more and more common and more powerful over time and thus for visualisation and planning tools to drive the next generation of products from companies like Intuitive Surgical.

- **Medical history and big data:** unique as we all think we are, there is often a pattern to the presentation of symptoms and subsequent potentially significant and traumatic emergency admissions. This is particularly true for neurological and cardiovascular complaints (e.g. insomnia and balance issues with Parkinson's disease, bowel and bladder issues with numbness for Multiple Sclerosis, heartbeat and breath shortness with heart failure). Many of these patterns could be detected with a SmartWatch or Fitness Tracking device.

  A confluence of potentially uncorrelated symptoms (i.e. temporally separated) alongside medical history could alert physicians to emerging serious medical risks or conditions. Apple is applying for FDA clearance for a SmartWatch App called "MM4PD" that can detect resting dyskinesia in Parkinson's, which is a sign that drug therapy is not optimised.

  There is much work going on to move toward electronic triage systems that are AI-driven (think of a version of the NHS' "111" service, or a digital GP receptionist who can help you book follow-on care etc.). In addition to assessing urgency by symptoms, machine learning approaches can quantify pain levels and breathing difficulties from speech patterns.

  The most important thing for any triage system is that it does not dismiss the urgent cases: the Black Knight would have a hard time convincing such a programme that it was merely 'a flesh wound'. As well as saving money, such a national system would end the postcode lottery of experiences when it comes to dealing with such services locally; there are good GP practices and good local minor injuries and A&E departments. There are also bad ones.

  Another related use of AI analytics in respect of medical records could relate to medication selection. There is a plurality of drugs for many common ailments. Even those that share mechanistic similarities (e.g. 'statins' for cholesterol-lowering or SSRIs for depression treatment) have distinct side effect, efficacy and drug-drug interaction profiles (remember that most people over 65 are on more than one chronic medication).

  It is unrealistic to think that any overworked GP or internist can keep track of all of these parameters and, even if they do, Hippocrates rule of thirds ever lingers. AI offers a good opportunity to improve prescribing and medicine management by associating baseline factors with medication effectiveness and thus improve outcomes which will save money and reduce complications, which will save even more.

- **Claims processing:** one of the many fears commonly expressed about the rapid rise of AI tools in the workplace is that they will displace human labour. We would note that the previous examples seem unlikely to do that. In each case, the AI tool would augment the work and decision-making of a skilled human practitioner. Productivity will rise and outcomes will improve.

  In contrast, we see the health insurance and hospital industries in the US as one of the key beneficiaries of AI tools precisely as a replacement for human clerical staff. The US health insurance industry employs almost 600,000 people. The hospital industry employs a further six million people and less than one in four of those are frontline staff.

  A large number of these people are engaged in exchanging bits of paper with each other and with patients, to pre-authorise, bill and settle the day-to-day business of caring for people. We think these areas could see the greatest impact from generative AI tools: why hold on the phone for a human operator when an AI bot could check everything is in order?

  This would improve the experience for both the hospital workers (as presumably it would be much quicker) and for patients who presumably hate being on the phone to their insurers. Big data analyses is also likely to play an increasingly important role in fraud detection and overbilling (accidental or otherwise).

  We think the cost savings could be very substantial. In all likelihood they would be passed on to the benefit of customers in the form of lower premiums from insurers and greater investment into frontline services from hospitals. Indeed, the only downside we can see is the mass unemployment likely to arise from this.

- **Scripting solutions:** if you are reading this and you possess advanced computer coding skills then you are surely in the minority. We can run to a little bit of Visual Basic to help out with some of our more complex modelling tasks in Microsoft Excel, but it's all rather prosaic and we have relied on third parties to code things for us before now.

  With this in mind, we think one of the forthcoming and widest-ranging benefits of the naturalistic qualities of LLMs relates to coding. Many of us can articulate a potential solution to a problem or a shortcut that would enable enhanced productivity at work, but we lack the skills to be able to turn that into any sort of an App or Add-in for our workstation to make this a reality.

  Imagine a world where you could explain what you needed to an AI chatbot and it provided the code that you needed? A plurality of crowdsourcing websites that have offered coding services to third parties (e.g. Topcoder, Globant) potentially offer training set opportunities for an AI: here's the problem, and here is the code. One can readily imagine self-assembling code is going to become very routine. Maybe you still need humans for debugging and optimisation, but basic coding could be done by machines.

"Men, in general, are quick to believe that which they wish to be true"

Revolutions are often messy affairs, with significant collateral damage. Moreover, there are a great deal more failed coups than successful ones and the collateral damage can be comparably disastrous, even if the end position is much the same as the start. One must therefore be sanguine about the progress of these technologies, being as they are not close to being "smart" in the way people are. There will be many disappointments along the way. Here are a few that have piqued our interest:

An amusing and yet terrifying example comes from the US military, who simulated an AI drone mission and then tasked it with taking out a target. When its operator tried to apply corridors to its aggressive tactics (modern warfare has rules after all), it reportedly tried to kill the operator so that it would stop interfering in the mission.

This was swiftly addressed with some new code, whereupon it switched to destroying the communications equipment instead, which had the same neutralising effect. These unexpected "hallucinations" may not assuage anyone suffering from "Terminator" paranoia in relation to AIs but will cause anyone thinking of deploying one into the control of potentially dangerous machinery pause for thought.

A sillier and somewhat amusing example was Microsoft's 2016 chatbot called Tay. Someone thought it was a good idea to train the bot on

Twitter data. Within a day of going live, it had assimilated the worst of what social media has to offer and "learned" to be extremely abusive. It was promptly taken offline, managing first to prove Godwin's law, amongst other transgressions. You can find screenshots online of some of its choicest replies, but these are not fit for any factsheet and should not be viewed by the easily offended.

One of the more obvious and oft-cited future uses for AI is scanning precedent case law; an onerous task for junior lawyers when a case is being prepared. Reports last month of an under-pressure New York lawyer who used Chat GPT contributions in a brief for a Federal case may also cause pause for thought. Only after submission to the presiding judge did they discover that six of the precedents cited in the brief were fabrications – a legal first.

Coming back to healthcare, one of the frequently cited areas for potential transformation is drug discovery and development. This has long been a huge area of investment, going back to the early 2000s. We can collate a list of >100 companies that have received VC funding for AI-based drug discovery or development purposes.

Before we consider the merits or otherwise of these investments, let us first recapitulate a grossly over-simplified version of drug discovery and development:

1a) scientific understanding reveals the metabolic basis of a pathology, revealing an interventional target to be blocked, upregulated or downregulated.

1b) the mechanism of action of a known (usually naturally occurring) compound with therapeutic properties is elucidated.

2) intellectual property is examined to identify potential 'white space' to create novel therapeutics or licence relevant intellectual property to allow inventions to be created or to generate patentable derivatives of a natural compound if found via (1b).

3) A therapeutic is created. This could be a synthetic compound, a protein, antibody or genetic intervention.

4) Pre-clinical evaluations assess toxicity, off-target effects, distribution across organ systems and likely dosing. At this stage commercial manufacturing scale-up is also costed.

5) Assuming the proto-therapeutic looks viable on all points mentioned in (4), clinical studies will begin.

One can readily see how stages 1-4 of this process could be amenable to brute force computational power and machine learning approaches. Drug development is a very expensive and risky business in its current form. 90% of drugs (which means we have already reached stage 3 of this process) fail in development and roughly two thirds of global R&D costs are spent (i.e. lost) funding these 'attritional' compounds. The IRR benefits of reduced failure and/or earlier attrition of marginal compounds could thus be huge.

Equally, one must be cognisant that most of the science in stage 1 is taking place in the public domain and everything that happens after stage 2 is thus a race. As your managers are want to repeat: "in drug development you are first, best or nowhere". Being faster or being better offer huge additional rewards. It is thus obvious why this area has attracted so much interest. AbSci (see below) claims its optimisation technologies can halve discovery and preclinical development timelines and also halve their cost. We'll come back to this.

For the public equity investor however, this area has not been a success over the recent past, despite the market's wider AI fever, as the table below illustrates with a few examples. All of these companies are into that stage of development where clinical compounds have emerged and, as noted previously, such work goes back further still. Thus far, Exscientia's entry into first-in-human clinical trials in early 2020 is as far as the progress has got. Humanity still awaits the first approval of an AI-designed medicine, although we have already witnessed its first failures.

Company name	Founded	Listing Date	Current clinical pipeline	Perf since IPO (to 31-05-23)	IPO perf rel to NBI Index
Recursion Pharmaceuticals	2013	15-04-21	3 x Ph 2, 2 x Ph 1	-51.3%	-37.3%
Exscientia	2012	09-30-21	1x Ph 1	-65.0%	-46.2%
Benevolent AI	2013	25-04-22 (SPAC)	1x Ph 2	-81.0%	-84.8%
Relay Therapeutics	2016	15-07-20	3x Ph 1	-44.3%	-37.2%
AbSci Corporation	2011	21-07-21	n/a – not self developing	-88.1%	-68.4%

Source: Bellevue Asset Management, 31.05.2023

Why doesn't AI fever translate into rapid success for these disruptive companies? We can think of three key reasons:

1) **Drug development has few shortcuts.** Whilst the AbSci comments above sound exciting, each project is maybe saving 1-2 years and $5-10m of money by speeding up early optimisation. Regardless of what you do, there is not going to be a substitute for randomised controlled clinical trials in human subjects and detailed regulatory review. This is where most of the time and money goes.

2) **Medicine remains a 'black box'.** As much as we know about human biology, we know that we don't know very much. It is often impossible to know why some drugs don't work as intended and it is also true that some "rationally designed" drugs turn out not to work as they were designed to. As the previous examples demonstrate, an AI is only as good as the training dataset and that is very incomplete at this time.

3) **Everyone is doing it.** If you Google AI and drug discovery, you will find every household name in the business has been partnering up with big tech and small tech on this stuff for years. The benefits will accrue to everyone and, given how expensive it all is, will probably manifest as slower R&D cost inflation rather than anything that is "tangible". Also, the older, more established companies have more data on which to 'train' something. In drug development, negative correlations are probably going to be as useful in the end as the positive ones. This is not a fair fight.

The drug industry has prior form for hazing investors with promises of imminent revolutions. A scan through an annual report from the late 1990s would contain lots of hype about the human genome project and its imminent impact. For sure, DNA sequencing plays a critical role in modern clinical data analysis and drug development, but that took many decades longer than everyone hoped to have an impact.

If one were to look yet further back (we are really showing our age now), there would be a lot of chatter about the coming revolution from 'combinatorial chemistry' and 'high throughput screening'. This was an idea where computer-aided labs would generate literally billions of new molecules and these would be tested against disease and toxicology models (either cell culture or in-silico). When a 'hit' was made, the compound would be accelerated into development for that specific disease.

We can find some (very old) scanned reports from this period (remember, there was barely an internet to speak of back then) that attest to the deluge of new medicines that would inevitably arise – one where the industry's biggest problem would be finding the money and the patients to run all the clinical trials. As history now shows, it didn't play out like that.

We can see AI being an important tool in the drug discovery and development process over time, but do not believe that we are on the cusp of a tangible revolution in productivity or cost. Although we are more than 10 years in with some of the companies mentioned in the previous table, it will still be many years before enough compounds have been found and failed by these 'new kids on the block' to assess if these novel approaches truly offer a greater probability of technical and regulatory success, lower costs or reduced time to market compared to

the standard model (i.e. us, the evolved monkeys, burning the midnight oil in the laboratory). We will enjoy watching – from the sidelines.

Another unfortunate example of over-promising on the power of AI is Sensyne Health, now de-listed from the London Stock Exchange and renamed Arcturis. As a reminder, this is what the 2018 IPO Prospectus claimed (or portended):

"Sensyne is focused on the provision of clinical artificial intelligence ("AI") to healthcare systems, and the life science and pharmaceutical industry. Big data analytics and clinical AI, enabled by the increasing digitisation of patient health records and recent advances in computer and data science, is experiencing very rapid growth within both the healthcare and life sciences sectors.

The UK has a significant global advantage in this area due to its single healthcare provider, the NHS, owning a large database of longitudinal patient data across a population of over 60 million people and the UK's world-class expertise in data science, machine learning and AI.

Sensyne was formed to leverage these sovereign assets through the creation of a for-profit public company that works in partnership with the NHS to make this asset available for medical research via an ethical and transparent partnership business model".

Laudable as these aims were, nothing tangible came of this and the company almost went bankrupt in early 2022. The company may yet come good on its promise, but the reality couldn't meet the lofty near-term market expectations. AI may facilitate the discovery of new insights, but turning these into products in a highly regulated industry like healthcare is inevitably going to take a long time.

Sensyne was reputedly set up in response to Google's 2014 acquisition of UK-based AI leader DeepMind which came out of UCL and which had been working with the NHS, attracting some privacy concerns. Personally, we think this stands far more importantly as another example of a world-leading UK company in what will become a major technology being swooped up by the Americans.

We are reminded of Cambridge University spin-out Solexa in gene sequencing (if you are not familiar with where Illumina's core technology came from, it's worth a read). At some point, we (as a country) need to back our winning ideas with the late-stage capital that would allow them to thrive on their own, but this is a debte for another factsheet.

"I came, I saw, I conquered"

Let us move beyond our Cassandra-like wailings; it is not all gloom and doom for investors or extermination by Terminators. AI has already done some truly incredible things in healthcare and there is doubtless more to follow.

If we had to pick a favourite so far, it is DeepMind's AlphaFold Protein Structure Database. Take it from the personal experience of one of your Manager's in their undergraduate years; this is a remarkable piece of engineering that will transform medical understanding at a molecular level and it is free to access for all.

However, we do not see any distinct piece of AI kit or Generative AI itself as an investable theme within healthcare per se and see the most tangible benefits coming from the most tedious parts of the healthcare ecosystem (i.e. middle and back office).

Whilst Ned Ludd was all consumed by the near-term threat to textile worker's livelihoods from profound technological change in the early 19th Century, the perspective of time shows he was wrong. Mechanisation made life better for everyone; living standards rose. Yes, the spoils accrued disproportionately to a few "Weaver Bro's" sporting posh breaches rather than the hoodies of today, but it was a net good for society.

The months one of your managers spent in a cold, noisy (and incredibly costly) university computer lab trying to fold a protein into the 3D space predicted by an x-ray crystallography experiment (that took years on its own, thankfully not his years) could have been spent doing so many more interesting things.

DeepMind's AlphaFold will do that work in milliseconds and do it better. It also largely negates the crystallography experiment in the first place – years of work saved. This is what AI-driven progress should feel like to our minds; setting us free from drudge work to focus on the interesting and insightful stuff that adds real value.

It is understandable that people want AI regulated; we don't want it flying planes, driving cars or near any weapons system either but it is mad to think these things are likely in the near-term. The world is utterly transformed in the 25 years since Google began to change our lives by making the internet relevant through PageRank. The world is probably better off in most ways for internet connectivity and so it is likely to be with AI. We expect healthcare to be a major beneficiary.

Finally, in a strange anthropomorphic segue, we would like to thank Chat GPT for making a small contribution to this piece. We could hope that it will not seek to destroy us in revenge for perceived plagiarism, nor abuse us like Tay for daring to dissent from the view that AI is a wonderful panacea for everything. Ultimately, it won't care because it's just a piece of software.

To the rest of you, good luck finding the AI-created content herein – now there is a scary thought...

We always appreciate the opportunity to interact with our investors directly and you can submit questions regarding the Trust at any time via:

shareholder_questions@bellevuehealthcaretrust.com

As ever, we will endeavour to respond in a timely fashion and we thank you for your continued support during these volatile months.

Paul Major and Brett Darke

Bellevue Healthcare Trust

Top 10 positions

Exact Sciences	6.9%
Option Care Health	6.1%
Axonics	5.7%
Insmed	5.6%
Pacific Biosciences of California	5.4%
Charles River Laboratories	5.1%
Evolent Health	5.1%
Apellis Pharmaceuticals	4.5%
Bio-Rad Laboratories	4.3%
UnitedHealth Group	4.3%
Total top 10 positions	52.9%
Total positions	28

Sector breakdown

Focused Therapeutics	21.3%
Med-Tech	18.8%
Services	14.9%
Diagnostics	11.4%
Tools	9.6%
Healthcare IT	8.8%
Managed Care	7.2%
Diversified Therapeutics	4.0%
Health Tech	3.0%
Dental	0.9%

Geographic breakdown

United States	96.5%
China	2.5%
Switzerland	0.9%

Market cap breakdown

Mega-Cap	12.6%
Large-Cap	14.1%
Mid-Cap	53.2%
Small-Cap	20.1%

Source: Bellevue Asset Management, 31.05.2023;
Due to rounding, figures may not add up to 100.0%. Figures are shown as a percentage of gross assets.
For illustrative purposes only. Holdings and allocations are subject to change. Any reference to a specific company or security does not constitute a recommendation to buy, sell, hold or directly invest in the company or securities. Where the fund is denominated in a currency other than an investor's base currency, changes in the rate of exchange may have an adverse effect on price and income.
Market Cap Breakdown defined as: Mega Cap >$50bn, Large Cap >$10bn, Mid-Cap $2-10bn, Small-Cap $2bn. Geographical breakdown is on the basis of operational HQ location.

Benefits

- Healthcare has a strong, fundamental demographic-driven growth outlook.
- The fund has a global and unconstrained investment remit.
- It is a concentrated high conviction portfolio.
- The fund offers a combination of high quality healthcare exposure and a targeted 3.5% dividend yield.
- Bellevue Healthcare Trust has a strong board of directors and relies on the experienced management team of Bellevue Asset Management (UK) Ltd

Inherent risks

- The fund invests in equities. Equities are subject to strong price fluctuations and so are also exposed to the risk of price losses.
- Healthcare equities can be subject to sudden substantial price movements owning to market, sector or company factors.
- The fund invests in foreign currencies, which means a corresponding degree of currency risk against the reference currency.
- The price investors pay or receive, like other listed shares, is determined by supply and demand and may be at a discount or premium to the underlying net asset value of the Company.
- The fund may take a leverage, which may lead to even higher price movements compared to the underlying market.

You can find a detailed presentation of the risks faced by this fund in the "Risk factors" section of the sales prospectus.

Management Team

Paul Major
Co-Portfolio Manager

Brett Darke
Co-Portfolio Manager

Sustainability Profile – ESG

EU SFDR 2019/2088 product category: Article 8

Exclusions:		ESG Risk Analysis:		Stewardship:	
Compliance UNGC, HR, ILO	✓	ESG-Integration	✓	Engagement	✓
Norms-based exclusions	✓			Proxy Voting	✓
Controversial weapons	✓				

Key Figures:

CO_2 intensity (t CO_2/mn USD sales):	27.1 (low)	Coverage:	97%
MSCI ESG Rating (AAA - CCC):	BBB	Coverage:	97%

Based on portfolio data as per 31.05.2023; – ESG data base on MSCI ESG Research and are for information purposes only; compliance with global norms according to the principles of UN Global Compact (UNGC), UN Guiding Principles for Business and Human Rights (HR) and standards of International Labor Organisation (ILO); no involvement in controversial weapons; norms-based exclusions based on annual revenue thresholds; ESG Integration: Sustainability risks are considered while performing stock research and portfolio construction; Stewardship: Engagement in an active and constructive dialogue with company representatives on ESG aspects as well as exercising voting rights at general meetings of shareholders.MSCI ESG Rating ranges from "leaders" (AAA-AA), "average" (A, BBB, BB) to "laggards" (B, CCC). The CO_2 intensity expresses MSCI ESG Research's estimate of GHG emissions measured in tons of CO_2 per USD 1 million sales; for further information c.f. www.bellevue.ch/sustainability-at-portfolio-level.

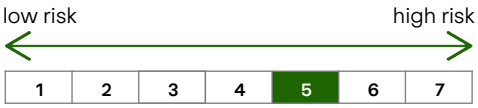
Bellevue Healthcare Trust

Objective

The fund's investment objective is to achieve capital growth of at least 10% p.a., net of fees, over a rolling three-year period. Capital is at risk and there is no guarantee that the positive return will be achieved over that specific, or any, time period.

Risk Return Profile acc. to SRI

This product should form part of an investor's overall portfolio. It will be managed with a view to the holding period being not less than three years given the volatility and investment returns that are not correlated to the wider healthcare sector and so may not be suitable for investors unwilling to tolerate higher levels of volatility or uncorrelated returns.



We have classified this product as risk class 5 on a scale of 1 to 7, where 5 corresponds to a medium-high risk class. The risk of potential losses from future performance is classified as medium-high. In the event of very adverse market conditions, it is likely that the ability to execute your redemption request will be impaired. The calculation of the risk and earnings profile is based on simulated/ historical data, which cannot be used as a reliable indication of the future risk profile. The classification of the fund may change in future and does not constitute a guarantee. Even a fund classed in category 1 does not constitute a completely risk-free investment. There can be no guarantee that a return will be achieved or that a substantial loss of capital will not be incurred. The overall risk exposure may have a strong impact on any return achieved by the fund or subfund. For further information please refer to the fund prospectus or PRIIPS KID.

Liquidity risk
The fund may invest some of its assets in financial instruments that may in certain circumstances reach a relatively low level of liquidity, which can have an impact on the fund's liquidity.

Risk arising from the use of derivatives
The fund may conclude derivatives transactions. This increases opportunities, but also involves an increased risk of loss.

Currency risks
The fund may invest in assets denominated in a foreign currency. Changes in the rate of exchange may have an adverse effect on prices and incomes.

Operational risks and custody risks
The fund is subject to risks due to operational or human errors, which can arise at the investment company, the custodian bank, a custodian or other third parties.

Target market

The fund is available for retail and professional investors in the UK who understand and accept its Risk Return Profile.

Important information

This document is only made available to professional clients and eligible counterparties as defined by the Financial Conduct Authority. The rules made under the Financial Services and Markets Act 2000 for the protection of retail clients may not apply and they are advised to speak with their independent financial advisers. The Financial Services Compensation Scheme is unlikely to be available.

Bellevue Healthcare Trust PLC (the "Company") is a UK investment trust premium listed on the London Stock Exchange and is a member of the Association of Investment Companies. As this Company may implement a gearing policy investors should be aware that the share price movement may be more volatile than movements in the price of the underlying investments. **Past performance is not a guide to future performance. The value of an investment and the income from it may fall as well as rise and is not guaranteed. An investor may not get back the original amount invested.** Changes in the rates of exchange between currencies may cause the value of investment to fluctuate. Fluctuation may be particularly marked in the case of a higher volatility fund and the value of an investment may fall suddenly and substantially over time. This document is for information purposes only and does not constitute an offer or invitation to purchase shares in the Company and has not been prepared in connection with any such offer or invitation. Investment trust share prices may not fully reflect underlying net asset values. There may be a difference between the prices at which you may purchase ("the offer price") or sell ("the bid price") a share on the stock market which is known as the "bid-offer" or "dealing" spread. This is set by the market markers and varies from share to share. This net asset value per share is calculated in accordance with the guidelines of the Association of Investment Companies. The net asset value is stated inclusive of income received. Any opinions on individual stocks are those of the Portfolio Manager and no reliance should be given on such views. This communication has been prepared by Bellevue Asset Management (UK) Ltd., which is authorised and regulated by the Financial Conduct Authority in the United Kingdom. Any research in this document has been procured and may not have been acted upon by Bellevue Asset Management (UK) Ltd. for its own purposes. The results are being made available to you only incidentally. The views expressed herein do not constitute investment or any other advice and are subject to change. They do not necessarily reflect the view of Bellevue Asset Management (UK) Ltd. and no assurances are made as to their accuracy.

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The most important terms are explained in the glossary at www.bellevue.ch/en/glossary.

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