GLOBAL LONG-TERM UNCONSTRAINED

MARTIN CURRIE
A Franklin Templeton Company

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For institutional, professional and wholesale investors only

INNOVATION OPPORTUNITIES IN HEALTHCARE

Medical technology and life science companies are benefiting from lifestyle shifts and demographic changes

Healthcare infrastructure is an important theme for us. The growing demand for healthcare infrastructure is driven by the trend towards an ageing population globally, leading to a greater need for healthcare spending over the coming decades.

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Demographics and modern lifestyle changes are increasing healthcare system costs. This combined with increasing regulatory pressure and complexity in product development are creating secular themes, challenges and opportunities within the sector. To help identify these, part of our fundamental analysis is centred on three long-term mega-trends: Demographic Changes, Future of Technology and Resource Scarcity.

Our approach to investing in healthcare is contextualised by our Long-Term Unconstrained (LTU) philosophy, and the companies we invest in to express these views. In this report, we discuss our preference for life science tools (LST) and medical technology (Med-Tech), relative to pharmaceutical and biotechnology companies, from a fundamental and thematic perspective. Taking a long-term approach and focusing on companies with high barriers to entry and dominant market positions, in our view leads to opportunities to own sustainable high growth and return businesses with low disruption risk and strong pricing power. These companies should compound cash flows at attractive rates, whilst having lower risk from leverage or poor governance.

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Focusing on sustainable quality growth healthcare companies

Our investment philosophy seeks to invest in companies with prospects of high returns on invested capital (ROIC), attractive revenues, earnings and cash-flow growth.

We believe healthcare companies operate within several structural themes that enable the best managed and positioned companies to generate superior growth and ROIC. High levels of complexity and regulation around products and services yield barriers to entry in the form of domain expertise, intellectual capital, high switching costs, and network effects. This creates the foundation for companies in the healthcare space to maintain a structural advantage. Organic re-investment creates a virtuous circle of innovation and economies of scale. As an example, **Illumina**, the market leader in next generation sequencing (NGS) within genomics, not only has the broadest, cheapest and most reliable offering of genomics instruments, but it has also built a hardware and software ecosystem across the entire sequencing workflow. Industry practitioners (researchers or bioinformaticians[1]) use Illumina's 'operating system' for both training and developing new research and products. Which they in turn can help improve, and Illumina can further automate. For example with artificial intelligence (AI), some of the data interpretation work saves its customers, such as large research labs or biotech companies, time and expense.

Generally, we do not find attractive stock ideas in biotechnology and pharmaceuticals due to regulatory, political, litigation, and pipeline risks, which can be difficult to forecast and/or assess through a fundamental lens. Historically egregious price increases for limited incremental innovation have drawn substantial political attention. This has been sharpened by healthcare systems facing extreme cost and utilisation pressures, worsened by the Covid-19 crisis. This increased attention further shifts the focus by payors on reimbursement; put another way, pharmaceuticals are incrementally a price-taker, rather than a price-maker, as demonstrated by the recently enacted Inflation Reduction Act (IRA) in the USA. This brings direct price controls to bear in drugs sold under US Medicare, although as usual, pharmaceuticals are litigating against these efforts.

[1]An individual that develops methods and software tools to understand biological data.

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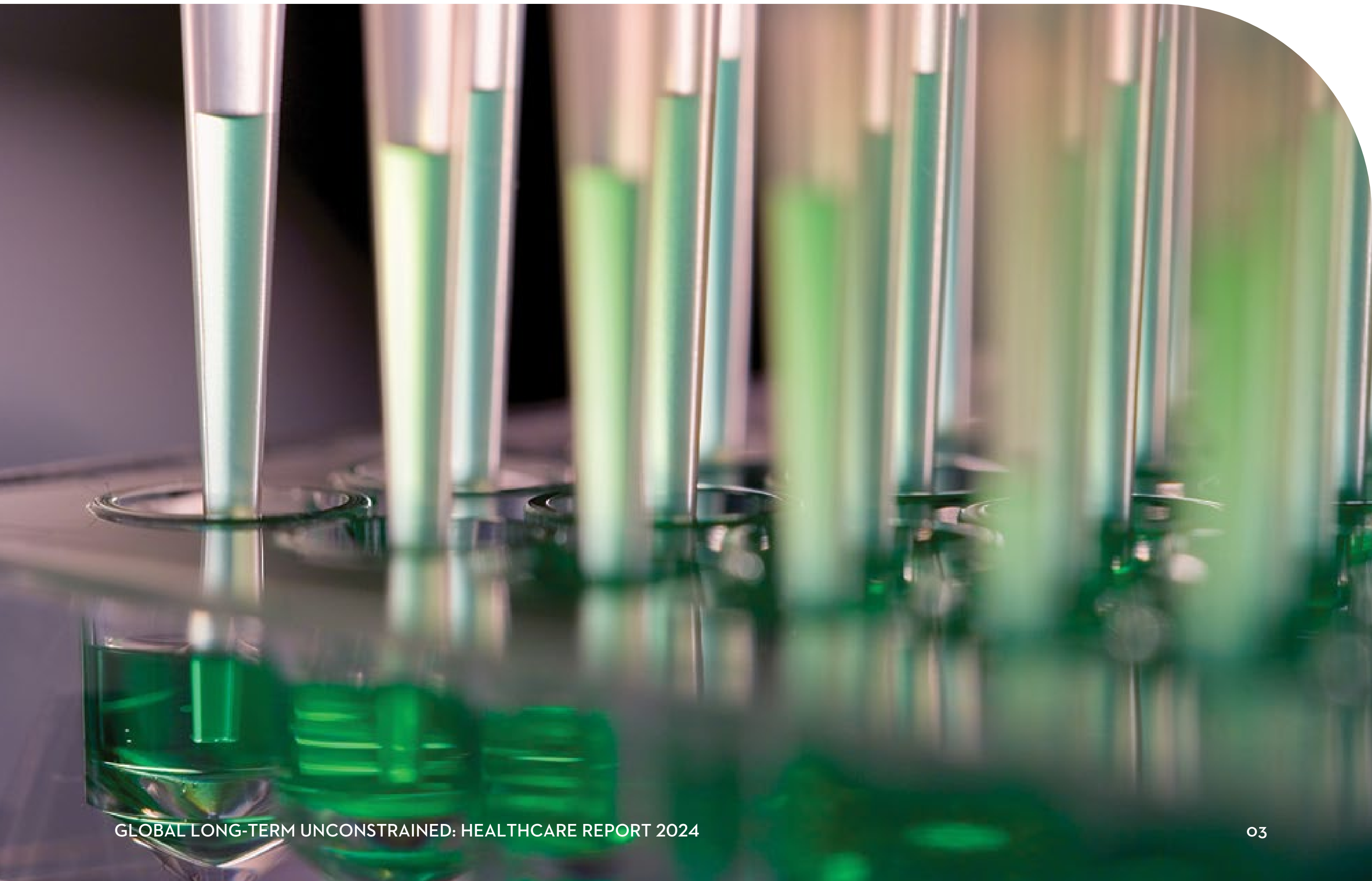
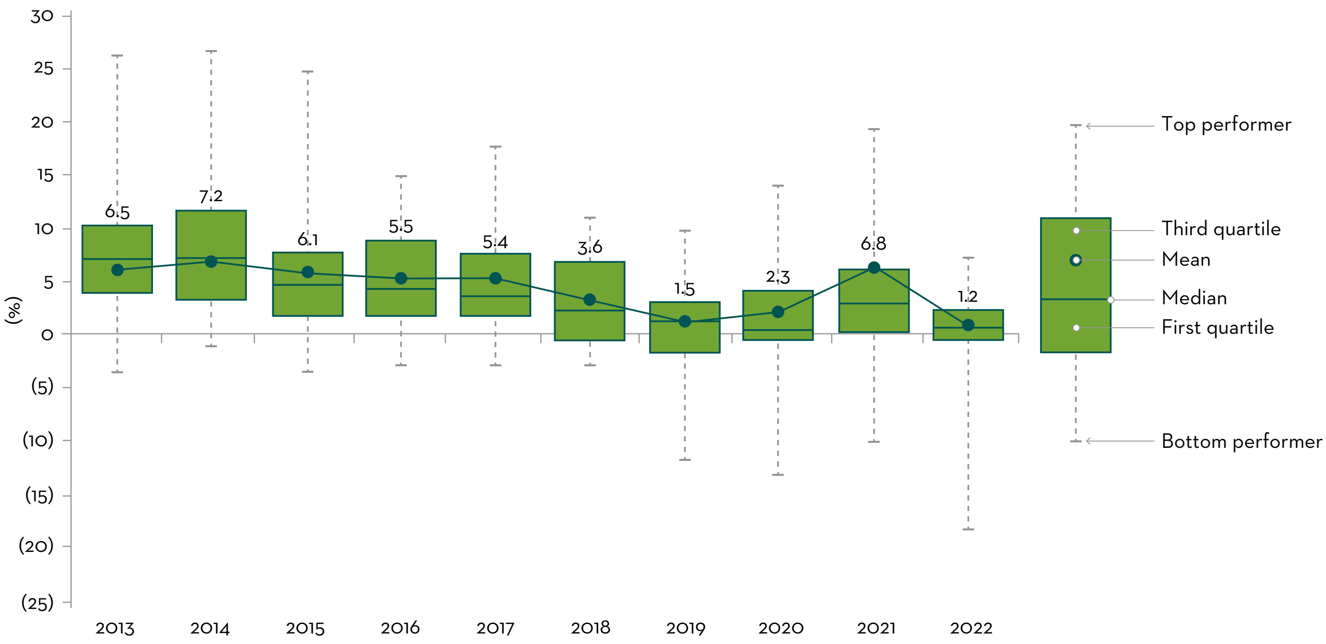


While the perception is that pharmaceutical company prices are increasing, net prices (i.e. after rebates to intermediaries) are decreasing to the tune of 3% per annum over the last five years[2], we believe this could worsen in the future in part driven by the IRA. Combined with research & development (R&D) clustering in certain areas such as oncology, this has intensified the competitive environment and degraded the economics of the industry. In general, current pharmaceutical ROICs are overstated, due to ongoing impairments of intangible assets generated from acquisitions, and reflect the return of on-market drugs, i.e. innovation that in some cases is 20 years old. We believe that, at an industry level, ROIC levels are closer to a range of 0 - 2%, similar to recent work by Deloitte[3] (who estimate 1.2%), which is far below the cost of capital for these businesses.

Pharmaceutical companies – return on late-stage pipeline, 2013-22 (ROIC %)



Source: Deloitte analysis, 2022. *2021 positively impacted by COVID.

Ageing populations and home care are creating structural growth opportunities

While some of the features of the healthcare market, such as regulation, can slow change and cause inertia, the growth opportunity remains attractive in an absolute and relative context. In our proprietary thematic framework, we see relevant, long-duration themes falling under all three of the mega trends of Demographic Changes, Resource Scarcity, and Future of Technology.

With inverted population pyramids across the developed, and increasingly developing world, society will face an ageing trend, which will lead to a healthcare cost problem. 22% of the global population will be over 60 by 2050[4] and in the US, the average annual healthcare spend on an over 65 year olds is 3.8 times higher than 18 to 45 year olds[5]. This is compounded by the growing epidemic of one of our key themes in **'Demographic Changes'**, **"21st century diseases"**, resulting from lifestyle choices (obesity and type 2 diabetes), living longer (Alzheimer's, dementia), or a combination of both, leading to an increased prominence of cancers.

[2]Source: Drug Channels, October 2023. Gross-to-Net Bubble Update: 2022 Pricing Realities at 10 Top Drugmakrers (rerun).

[3]Source: Deloitte as at 2023.

[4]Source: Word Health Organisation as at October 2022. Ageing and Health.
https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

[5]Source: Health System Tracker as at January 2024. How do health expenditures vary across the population.
https://www.healthsystemtracker.org/chart-collection/health-expenditures-vary-across-population/

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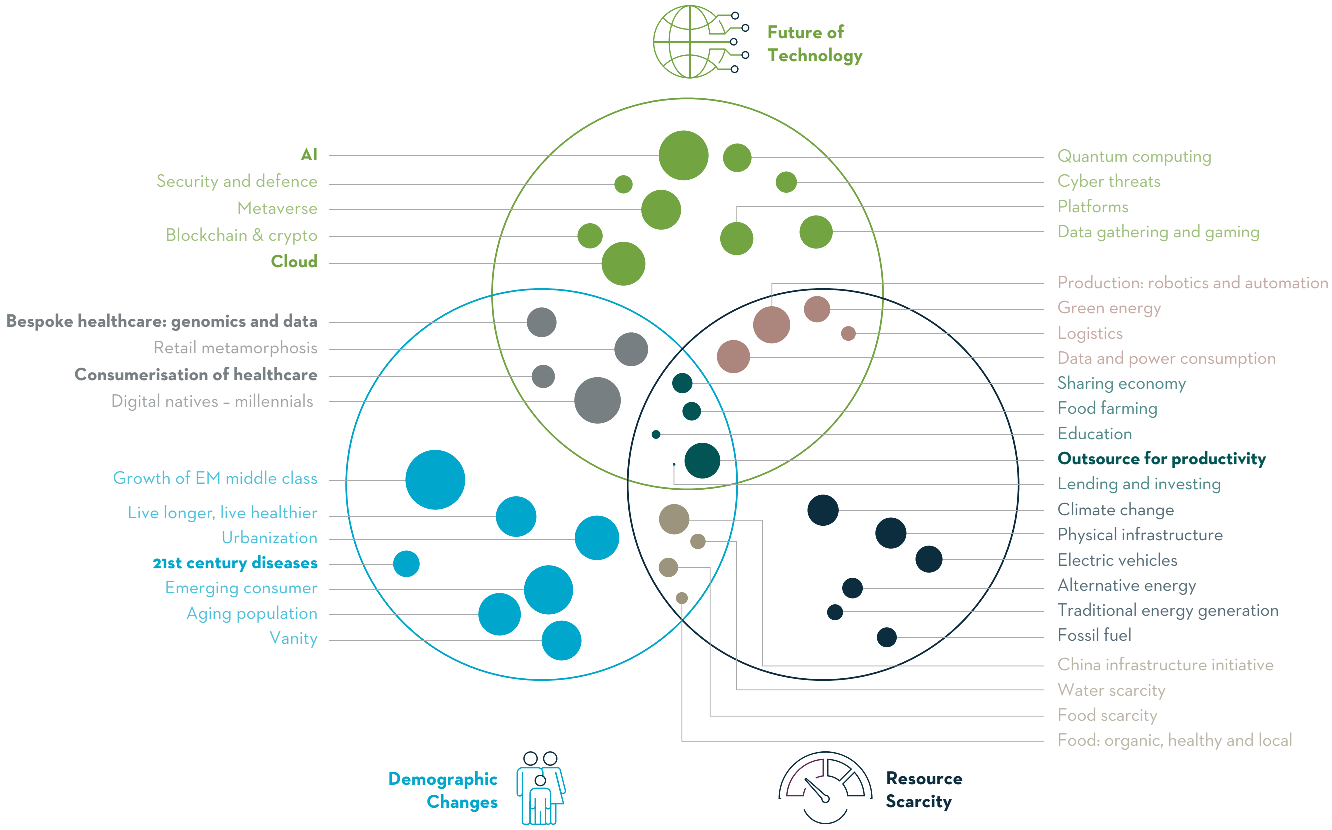
We see this increased incidence of diseases related to ageing trends and lifestyle leading to potential trends within two segments:

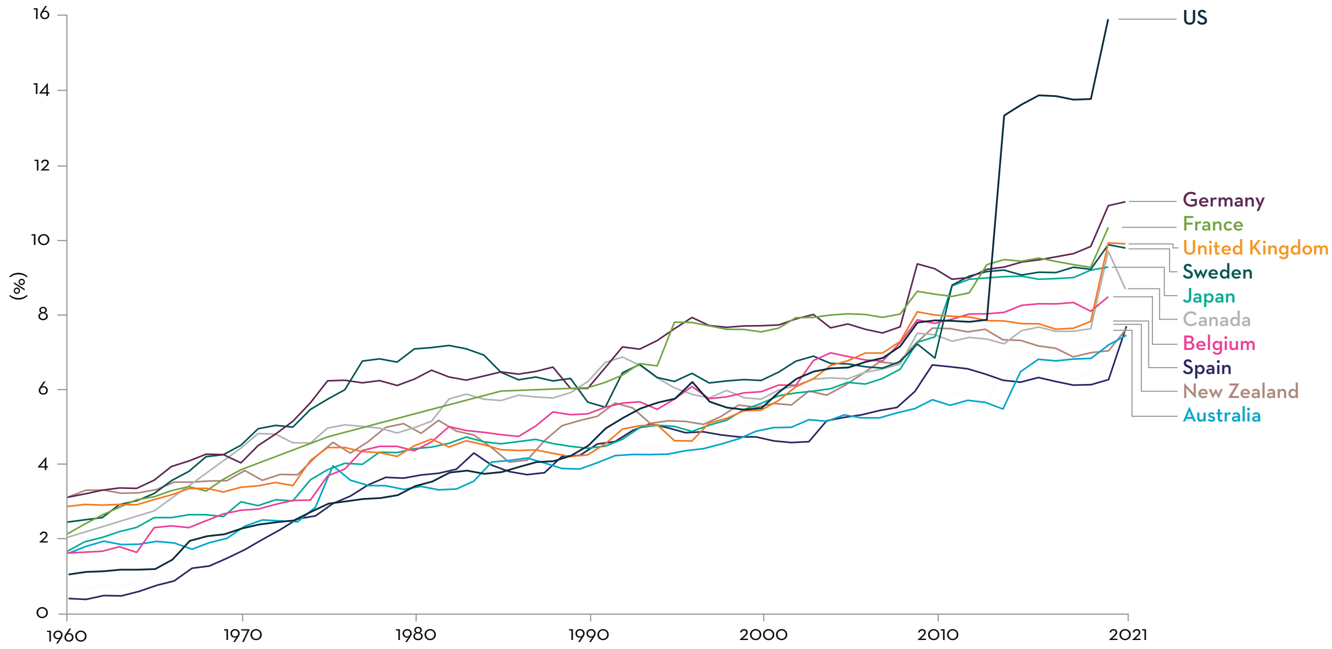
1. **Technology-driven solutions:** with breakthroughs in genomics enabling increasingly **bespoke healthcare**, fragmenting patient populations through personalised diagnostics and treatments such as gene editing.
2. **Efficiency-driven solutions:** including **outsourcing to productivity** and using **Cloud & AI** to drive **the consumerisation of healthcare**. Where patient care may move to lower cost settings such as the home, enabled by remote monitoring technology in devices including smartphones.



Source: Martin Currie as at 31 January 2023. Representative Martin Currie Global Long-Term Unconstrained account shown.

This persistent mismatch between healthcare demand and the infrastructure available to meet supply as a multi-decade backdrop, is evidenced by the persistent increase in healthcare expenditure as a percentage of Gross Domestic Product (GDP)[6].

Return on late-stage pipeline, 2013-22



Source: Our World In Data based on Lindert (1994), OECD (1993), OECD Stat as at 2021. *https://ourworldindata.org/grapher/public-health-expenditure-share-gdp*

Medical technology company **ResMed** provides cloud connected devices and software to treat breathing conditions including sleep apnea and chronic obstructive pulmonary disorder (COPD), both predominantly lifestyle driven diseases (obesity & smoking, respectively). The technology mitigates hospital capacity and cost impacts by allowing patients to receive care in the home while remaining under the supervision of medical practitioners. **Coloplast** sells disposable chronic care products, mostly to stoma surgery and continence care patients, often the result of cancers correlated to ageing. These products enable patients to recover much of their quality of life, while again saving the healthcare system substantial cost by moving patients out of expensive healthcare settings such as hospitals and assisted care facilities, to the home.

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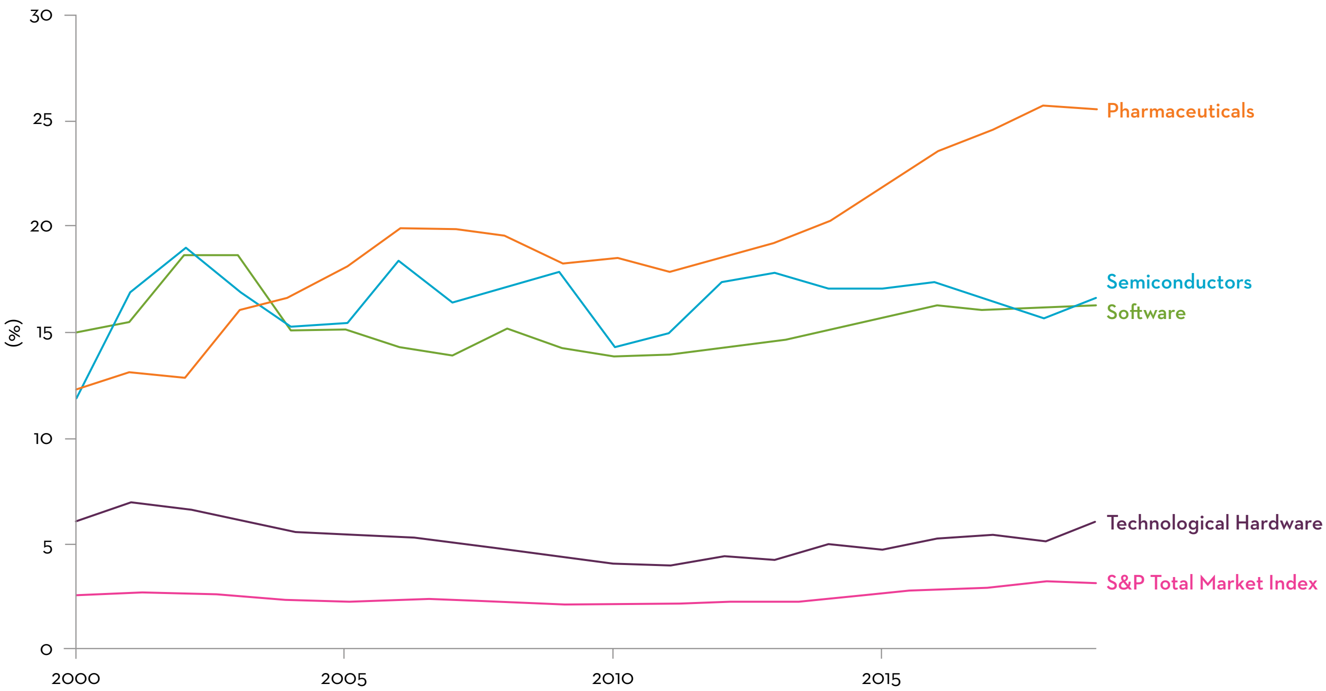
Medical technology and life science companies can better harness increasing R&D

One manifestation of these growing healthcare trends is in drug development expenditure.

As the scientific low-hanging fruit has been captured in simpler, small molecule drugs, increased complexity means the average development cost per on-market drug increased in 2022 by US$298 million, to US$2.3 billion[7]. Simultaneously, new drug modalities, such as gene therapies, have to overcome more stringent regulatory hurdles, target smaller patient cohorts, and face less favourable reimbursement environments.

Average R&D Intensities for Publicly Traded US Companies, by Industry



Source: Congressional Budget Office using data from Bloomberg, limited to US firms as identified by Aswath Damodaran, 'Data Breakdown' (accessed 13 January 2020).

As pharmaceuticals and biotechnology companies invest behind this less productive innovation, R&D intensity necessarily increases (now 20.4% on average, according to PhRMA[8]), as does total expenditure (6.7% compound annual growth rate 2014-22, according to EvaluatePharma). Therefore drug originators must offset a compression of their returns through other means. On this basis, we see the drug development and commercialisation value chain as an attractive source of opportunities that offer mission-critical solutions for complexity and efficiency. This applies to our portfolio holdings in **Illumina**, **Sartorius Stedim**, **Mettler Toledo** and **Veeva**.

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[7]Source: Deloitte as at January 2023. Pharma R&D return on investment falls in post-pandemic market.
https://www2.deloitte.com/uk/en/pages/press-releases/articles/pharma-r-d-return-on-investment-falls-in-post-pandemic-market.html

[8]Source: PhRMA. 2023 PhRMA Annual Membership Survey.

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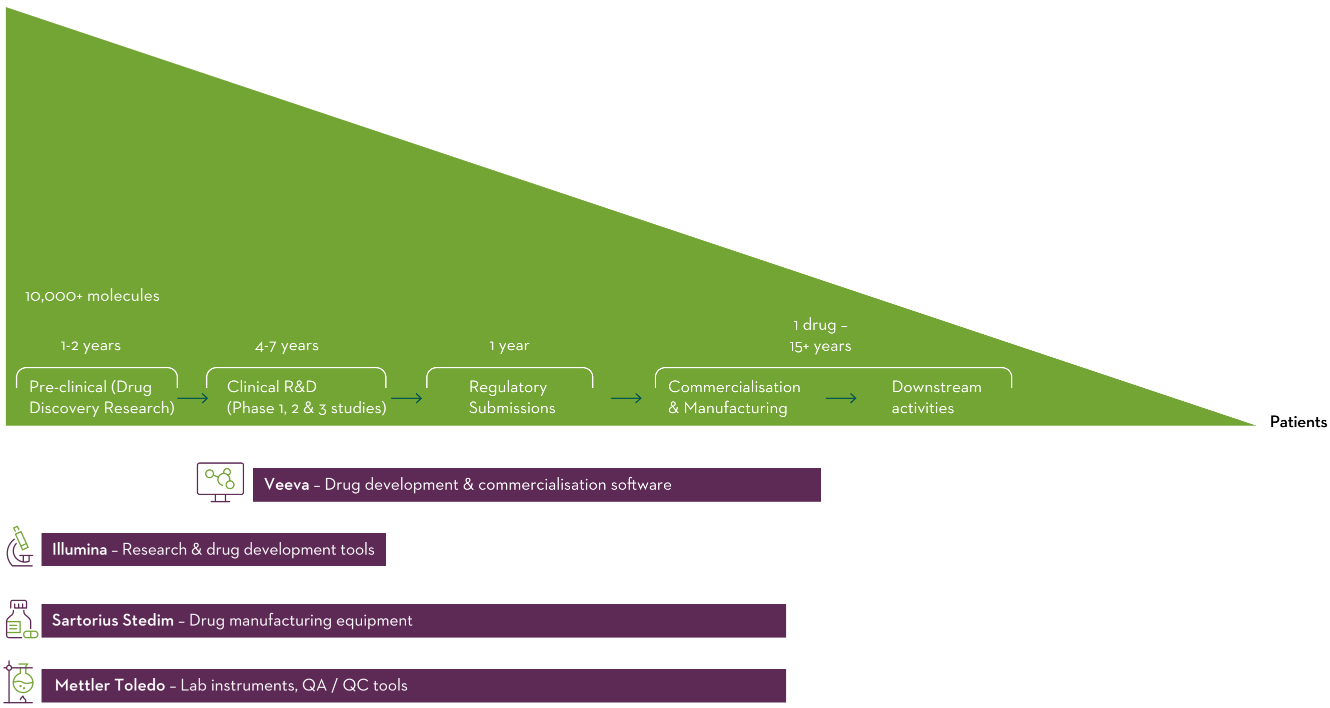
Sartorius Stedim is the single-use bioprocessing (SUT) market leader with 30% share. It provides biologic, cell and gene therapy (CGT) drug manufacturing equipment, and recurring consumables to pharmaceutical, biotechnology and contract (outsourced) drug development customers. Single use technology is a superior offering for these faster growing modalities. These are often manufactured in smaller batches, lowering upfront capital expenditure and cleaning costs, allowing for greater production flexibility, and improving water and energy efficiency.

While we expect the overall pharmaceutical and biotech end markets to grow 5%+[9], the share of biologics is set to increase from 30% today to over 50%[10], with similar dynamics, from a lower base, for CGT. We believe Sartorius Stedim's biologics and CGT customer base are likely to outgrow the market, while the product mix from SUT will continue to increase. Stedim's strategic spending can also increase while still generating incremental growth in ROIC.

Mettler-Toledo also provides exposure to growth of the pharmaceutical and biotech end markets. As the leading global supplier of mission-critical precision balance instruments and services for life science (largely pharmaceutical), industrial and food industries, its growth derives from themes of higher regulatory requirements from quality assurance/control, amongst others.

Veeva Systems provides industry specific 'vertical' software as a service (SAAS) to aid biopharmaceutical customers with applications for drug development and commercial execution. Veeva is an enabler of customer efficiency, including vendor consolidation. While its breadth allows it to build the largest data assets across the industry, strengthening its product offerings, including emerging AI applications.

Drug value chain



[9]Source: Evaluate as at August 2023. Evaluate Forcasts Global Pharmaceutical market to be worth $1.6tn in 2028.
https://www.evaluate.com/about/press-releases/evaluate-forecasts-global-pharmaceutical-market-be-worth-16tn-2028

[10]Source: Martin Currie as at 31 December 2023.

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Attractive exposure to specialty pharmaceuticals and animal health

In general, we do not find attractive ideas in the pharmaceuticals space, preferring the market structure in certain areas of speciality pharmaceuticals and animal health.

We have completed extensive work in the diabetes and obesity disease area, here we see the sales generation, earnings growth and ROIC that fits our philosophy. Initially, we did not invest in these names as we underestimated the rate of penetration of the latest generation obesity drugs. For example, one obesity drug from a leading pharmaceutical firm has been on-market for over five years, and it achieved less than 1% uptake, with limited interest from both patients and importantly physicians. We, and the market, underestimated the inflection in physicians' willingness to prescribe drugs for weight loss, once a ~10% weight loss threshold was achieved. Specifically, the company in question was able to leverage its existing relationships with endocrinologists, used to prescribing its GLP-1 drugs for diabetes, and leverage this into a broader population. This was before awareness on social media grew exponentially, generating further demand well ahead of current levels of supply.

For the obesity pharmaceutical leaders to meet this demand, they need to cross several gating points.

This includes being able to:

- manufacture enough of the drug to meet a rapidly growing demand,
- have physicians write enough prescriptions, to have insurers reimbursing these prescriptions,
- have employers opting into insurance programs, and finally;
- have patients remaining adherent to their dosing regimen.

In our view, reimbursement coverage, the associated pricing concessions required, and patient adherence in a real-world setting (as opposed to clinical trial), are the three factors that introduce risk to the market's expectations for this attractive drug category.

We see **CSL** as a best-in-class specialty biopharmaceuticals with regulatory protection of its oligopolistic position in the blood plasma therapeutics business. Historical safety concerns, related to the collection of the plasma required to produce CSL drugs, means that there cannot be new entrants providing a more attractive market structure, which mitigates patent risk and reimbursement pressure. **Zoetis** and **Idexx Laboratories** are the market leaders, with 25% and 65% share in livestock and pet drug and diagnostic markets respectively. Relative to traditional human pharma, research is comparatively nascent, providing superior returns to R&D, with lower regulatory requirements and competition, which provide longer product cycles, and a more benign pricing environment when drugs go off-patent.

Focusing on leading companies to capture secular drivers

Demographics and lifestyle choices will drive decades-long need for innovation and efficiencies to meet healthcare demand that will consume an increasing proportion of GDP.

Companies with products and services addressing these needs stand to benefit from growth opportunities in attractive market structures. These firms are generally protected from the omnipresent threat of disruption coming from big-tech companies due to regulatory requirements and high domain expertise that can be further consolidated with emerging technologies like AI. As long term investors, we ensure that we capture these investment opportunities by focusing on companies with attractive structural growth prospects and the ability to generate high ROICs over the long-term. At the same time, we constantly keep valuation at the center of our evaluation process.

The companies detailed in the document represent all current healthcare holdings in our Global Long-Term Unconstrained strategy (as at 31 December 2023). Overall, this represents 23% of the portfolio, and a 12% overweight compared to MSCI ACWI. This makes healthcare our largest active sector exposure within the strategy.

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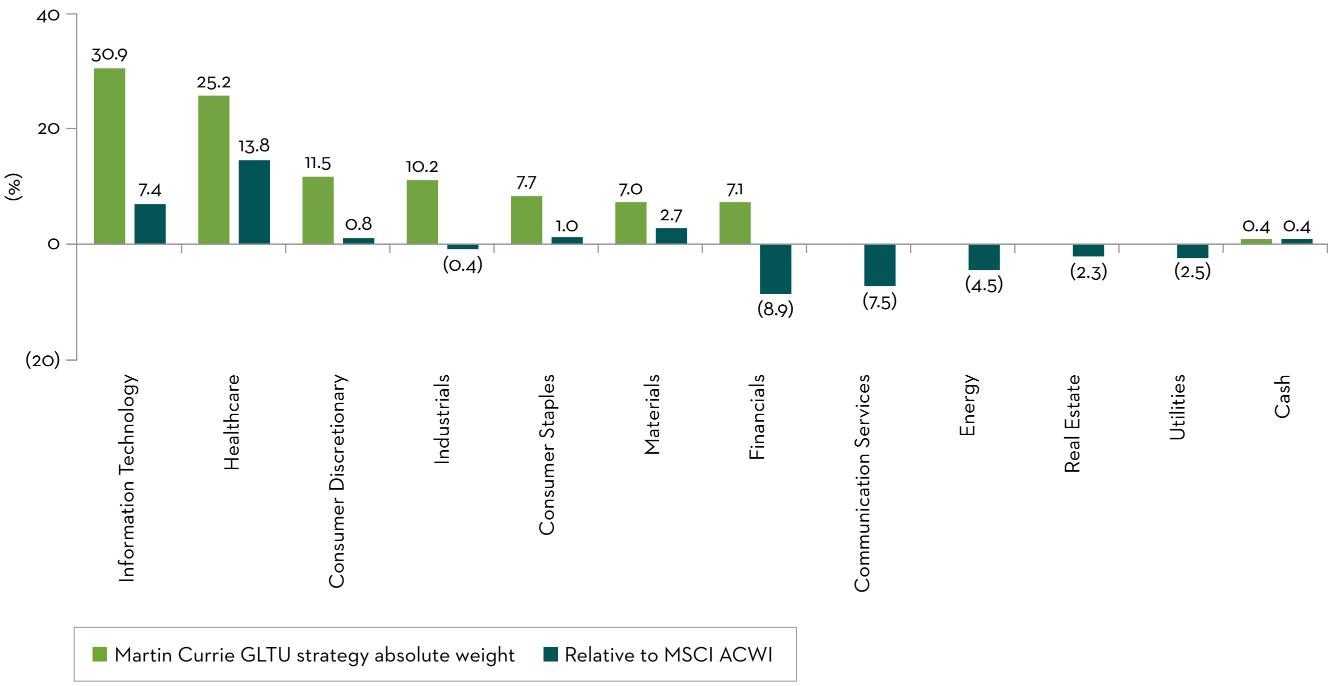
Appendix

GLTU strategy healthcare holdings

Stock	Country	Sub-sector	Portfolio (%)
Illumina	United States	Life Sciences Tools & Services	3.9
CSL	Australia	Biotechnology	3.2
Sartorius Stedim	France	Life Sciences Tools & Services	3.0
ResMed	United States	Healthcare Equipment & Supplies	2.8
Coloplast	Denmark	Healthcare Equipment & Supplies	2.7
Zoetis	United States	Pharmaceuticals	2.6
Mettler-Toledo	United States	Life Sciences Tools & Services	2.6
Veeva Systems	United States	Healthcare Technology	2.6
Idexx	United States	Healthcare Equipment & Supplies	2.0

Sector weights



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- This strategy may hold a limited number of investments. If one of these investments falls in value this can have a greater impact on the strategy's value than if it held a larger number of investments.
- Smaller companies may be riskier and their shares may be less liquid than larger companies, meaning that their share price may be more volatile.
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