

## Investing in Life-Changing Treatments: Compelling Opportunities Driven by a Patients-First Focus

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### Summary

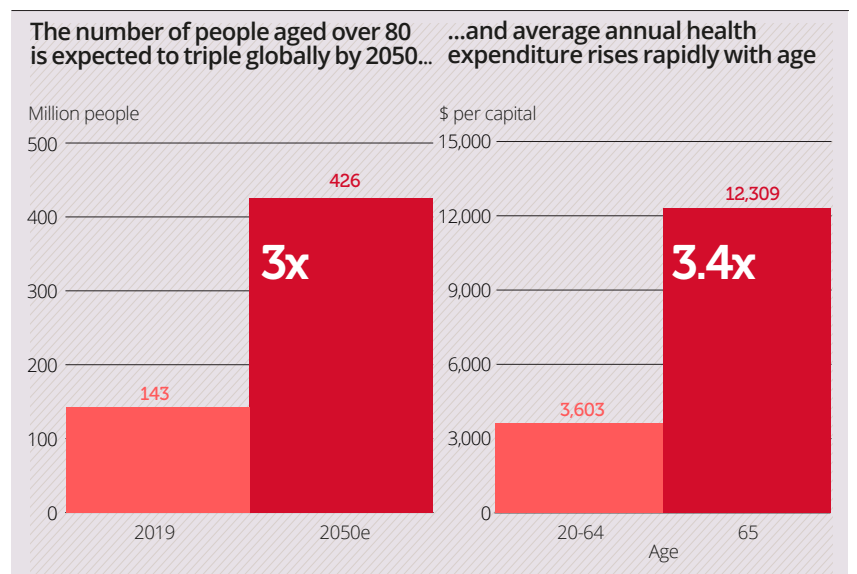
- We believe simply being innovative in healthcare is not enough, and focusing on companies that provide life-changing healthcare solutions realigns investing in healthcare by putting the core focus back on patients
- Life-changing treatments meaningfully advance the standard of care, increasing their value to key stakeholders and enhancing a company's potential to earn higher returns if they can optimise patient access
- Ultimately, a patients-first approach isn't just good from a human perspective, we believe it helps us identify companies that are more commercially compelling in order to maximise returns

Innovation is often revered when it comes to investing, including when it comes to the healthcare sector. We believe that offering innovative healthcare solutions is not enough, and in this white paper, we discuss why we believe patients – and what changes their lives for the better – will be key to companies achieving commercial success.

The world is facing various healthcare challenges. It is estimated that over half of the global population lacks access to essential health services<sup>1</sup>, and rising chronic disease prevalence and ageing populations ensure that even high-income countries are not immune.

A person's need for healthcare typically increases with age, and global populations are ageing much faster than in the past.

By 2050, the number of people over the age of 80 is forecast to triple to 426 million and there could be over two billion people over the age of 60, 80% of which will be in low- and middle-income countries.<sup>2</sup>



Sources: World Health Organization<sup>2</sup>, Papanicolas, I., et al. JAMA Network Open. 2020, 3(8): e2014688. The information shown above is for illustrative purposes only and is not intended to be, and should not be interpreted as, recommendations or advice.

<sup>1</sup> World Health Organization – Tracking Universal Health Coverage: 2023 global monitoring report

<sup>2</sup> <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health>; accessed on 18/12/2023

<sup>3</sup> Payers typically refers to health insurers or government-funded healthcare programs that pay for healthcare goods and services.

These structural megatrends and defensive characteristics from resilient demand underline the case for investing in healthcare, as well as growth potential from capitalising on advancements in technology. Yet, we believe this can unravel when innovation is idolised but does not translate into life-changing results for patients, making it less valuable to patients, physicians, payers<sup>3</sup> and policymakers.

We look for companies that provide life-changing healthcare solutions through focusing on three areas:

- Life-changing drugs
- Health system strengthening
- Life-changing care

We believe that taking this holistic approach and focusing on what truly matters to patients can lead to better outcomes for patients and, ultimately, greater commercial success.

### *Hang on, don't all healthcare investors focus on patients?*

Patients are unquestionably the most important stakeholder and the ultimate end consumer in healthcare, so surely it should be self-evident to investors that they are a core focus, right? In reality, we think investors' focus has drifted and many talk more about 'innovative' technologies like genomics and how that will drive 'change' than the actual relevance for patients.

**"The life-changing treatments approach is about realigning investing in healthcare, moving away from the trend of focusing on innovation and putting the core focus back on patients."**

### **Focusing on patients**

The life-changing treatments approach is about realigning investing in healthcare, moving away from the trend of focusing on innovation and putting the core focus back on patients, because we believe life-changing treatments for patients are more compelling commercial opportunities.

Putting the patient at the heart of a healthcare investment strategy isn't just good from a human perspective; we believe it allows us to identify more commercially compelling companies to maximise returns. Life-changing treatments meaningfully advance the standard of care, making them more valuable to patients, physicians, payers, and policymakers; and this gives companies that develop life-changing treatments the possibility to earn higher returns if they can optimise patient access.

Advancing the standard of care might involve curing a previously untreatable condition, improving the patient's experience of the care they receive or giving access to healthcare in a region where patients have been underserved.

### **The pitfalls of focusing on innovation**

The fate of the world's first approved gene therapy, Glybera, highlights the pitfalls of viewing investments through the lens of innovation rather than what matters most to patients. Glybera was approved by the European Medicines Agency in 2012 to treat rare disease lipoprotein lipase deficiency (LPLD) and was undoubtedly an example of first-in-class innovation. It was, however, a commercial disaster, selling only one dose before being pulled from the market by its manufacturer in 2017.<sup>4</sup>

Glybera faced significant challenges in commercialisation, perhaps the most important of which were questions surrounding the drug's impact on patients. A long-term study observed that while the drug reduced inflammation of the pancreas in up to 50% of patients, it didn't sufficiently eliminate this serious complication associated with LPLD.<sup>5</sup>

LPLD is a rare disease which can make it more challenging to find patients, but treating rare diseases can be commercially successful. For example, AstraZeneca has a successful rare disease franchise, with lead commercial drugs Soliris and Ultomiris selling more than \$5bn globally in 2022 by treating a number of rare diseases<sup>6</sup>.

Glybera also had a high list price, almost \$1m per dose. High costs are more common for rare disease drugs because of the low number of patients and the high costs of developing, testing, and launching drugs. However, a high list price does not prevent commercial success. Novartis sells rare disease drug, Zolgensma, with a list price of \$2.1m and, because of its strong patient benefit, reported net sales of over \$1.3bn in 2022.<sup>7</sup>

Glybera is an example of successful innovation, but investment failure because a return wasn't earned for the cost of developing the drug and funding clinical trials. The conclusion we draw from the example above is that a strong positive impact on patients and facilitating patients' access to treatments are more important factors for commercial success than simply being innovative.

Glybera isn't the only example of a therapy where innovation wasn't enough to deliver commercial success. In 2016, a new class of antibody-based drugs to treat high cholesterol known as PCSK9 inhibitor antibodies launched with high expectations for commercial success. Inhibiting PCSK9 with an antibody was undoubtedly an innovative approach and some analysts believed the PCSK9 class would generate \$5-10bn in total sales<sup>8</sup>, while others expected one of the drugs in the class, evolocumab, to reach more than \$1bn in sales by 2018.<sup>9</sup>

In reality, sales were well below expectations, with evolocumab reaching about half of the forecasted \$1bn in 2018. Payers balked at the higher cost of the PCSK9 drugs, particularly given the cost of widely used statins had fallen significantly since going off-patent. Further, there was a lack of clear evidence at launch of the benefits to patients in reducing the risk of heart attacks and strokes.

Ultimately, companies selling these drugs had to reduce prices<sup>10</sup> because payers were not convinced the benefits of these drugs to patients justified the higher cost. We believe the lesson here is that therapies need strong evidence to justify their price, particularly a positive life-changing impact on patients.

<sup>4</sup> <https://www.nbcnews.com/health/health-news/firm-pulls-world-s-first-gene-therapy-treatment-no-one-n748906> accessed on 23/08/2023

<sup>5</sup> Gaudet, D. et al. Hum Gene Ther. 2016, 27(11), 916-925

<sup>6</sup> Bloomberg, as at October 2023

<sup>7</sup> <https://www.novartis.com/investors/financial-data/product-sales> accessed on 21/08/2023

<sup>8</sup> Goldmans Sachs research note, 23/4/2014

<sup>9</sup> Jefferies research note, 27/01/2015; Piper Jaffray research note, 31/03/2014

<sup>10</sup> <https://www.fiercepharma.com/pharma/cholesterol-war-escalates-as-amgen-makes-60-price-cut-repatha-permanent>; accessed on 15/12/2023

Aducanumab is another example of an innovative drug that disappointed commercially. Aducanumab was the first new Alzheimer's disease drug to be approved in almost 20 years in the US<sup>11</sup>, but a commercial failure. Sales disappointed with Biogen reporting sales of just \$2.8mil the first quarter of 2023 and writing off about \$275mil of unsold inventory of the drug. The initial approval of the drug was controversial, with many physicians believing the benefit to patients shown in clinical trials was insufficient to justify even approving the drug in the first place.<sup>12</sup>

Aducanumab's failure should by now reflect a familiar theme: questionable efficacy and a higher price than many expected, demonstrating once again the perils of believing that innovation is the sole key to commercial success instead of positive life-changing impacts on patients.

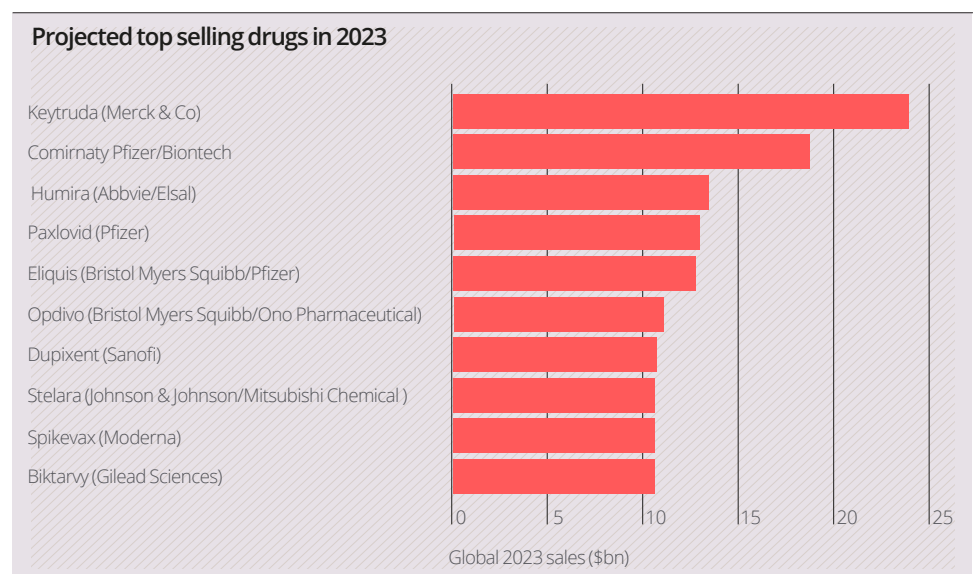
## The investment opportunity

As mentioned earlier, we see three opportunity sets when seeking companies delivering healthcare solutions that improve patients' lives:

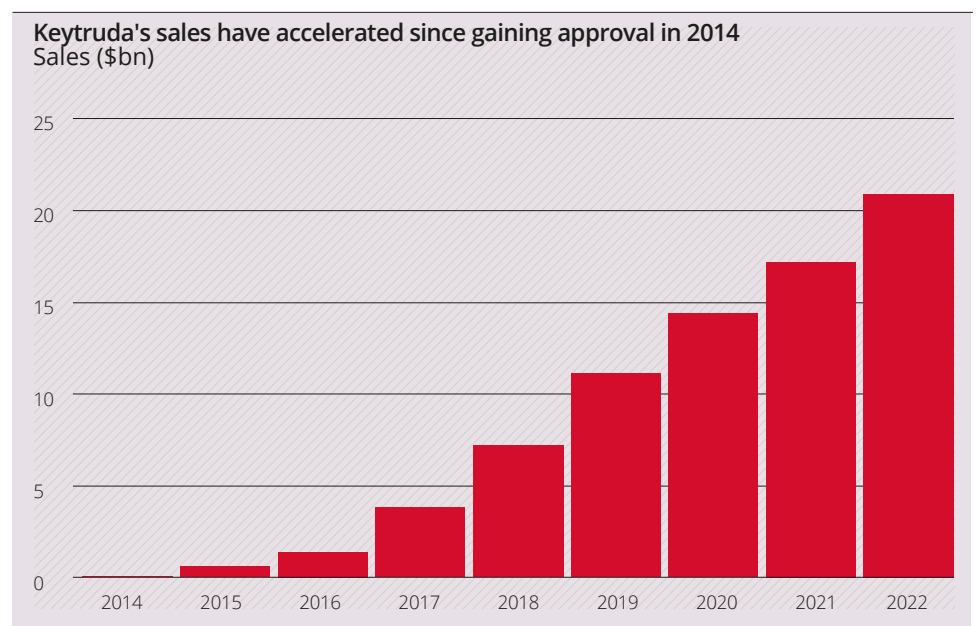
- Life-changing drugs
- Health system strengthening
- Life-changing care

### Life-changing drugs

We believe drugs that make a meaningful difference to patients' lives have a higher probability of commercial success. Within the theme of life-changing drugs, we include drugs that are changing medical practice today, such as anti-cancer drug, Keytruda, which harnesses the immune system to attack cancer cells and is forecast to be the biggest selling drug worldwide in 2023.<sup>13</sup>



Source: Evaluate Pharma and Evaluate Vantage as of January 2023. The information shown above is for illustrative purposes only and is not intended to be, and should not be interpreted as, recommendations or advice. Past performance is not a guide to future results.



Source: Merck, February 2023. The information shown above is for illustrative purposes only and is not intended to be, and should not be interpreted as, recommendations or advice.

<sup>11</sup> Lalli, G., et al. EMBO Mol Med. 2021, 13(8), epub

<sup>12</sup> <https://www.nytimes.com/2021/05/28/opinion/alzheimer-treatment-fda-aducanumab.html>; accessed on 15/12/2023

<sup>13</sup> <https://www.evaluate.com/vantage/articles/analysis/biggest-selling-drugs-2023> accessed on 18/07/2023

Keytruda, also known as pembrolizumab, is part of a class of drugs called immunotherapy because it harnesses the body's own immune system to fight cancer. Keytruda can be used across a range of cancers, and unusually for a drug approved in 2014, it continues to show new positive benefits for patients in clinical trials today.

During 2023's American Society of Clinical Oncology Congress, one of the world's largest meetings for researchers and doctors specialising in cancer care, data was presented showing Keytruda in combination with chemotherapy can significantly improve a patient's chance of survival from cervical cancer, leading one doctor to remark "I think it is probably possible to cure a solid tumor with immunotherapy."<sup>14</sup> The fact that doctors are talking about immunotherapy as a cure for cancer provides hope for millions worldwide.

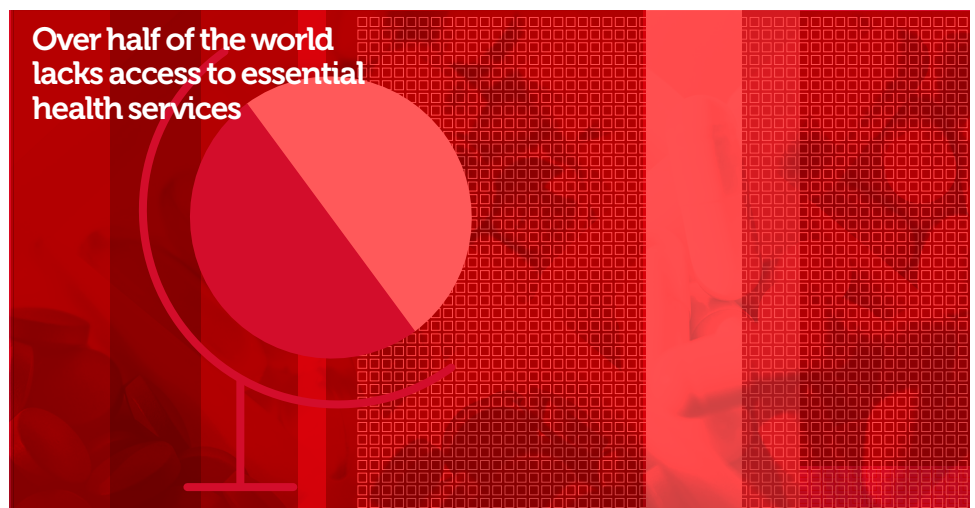
The theme also includes next-generation drugs, which are still in clinical trials, but have shown early and strong evidence of practice-changing potential. Finally, life-changing drugs also focuses on solutions to global health priorities such as Alzheimer's disease and antimicrobial resistance.

### Health system strengthening

The health system strengthening theme aims to address improving patients' lives by investing in companies that improve access to care, enable future innovations and improve diagnosis. Sometimes, even when treatments are available, other barriers prevent or delay a patient from getting optimal care.

We believe tackling issues around access to care will create additional growth opportunities for companies throughout the healthcare sector. The scale of the problem is huge: it is estimated that as many as 4.5bn people lack access to all the healthcare services they need worldwide (as of 2021)<sup>1</sup>.

Improving access to care could be increasing the number of hospital beds in underserved regions. Enabling future innovations that focus on new research tools and infrastructure and techniques which could open up new fields of research or increase drug production capacity are also critical to treating more patients. Further, it is not just about providing cures; improving diagnostic solutions that enhance the precision and timeline of treatment is also crucial in optimising patient care.



Source: World Health Organization<sup>1</sup>

### Life-changing care

Life-changing care focuses on health needs that aren't fully addressed with pharmaceuticals. If we take the US healthcare system as an example, only 10% of healthcare spending is on prescription drugs, so life-changing care focuses on the 90% of spending that goes into everything from hospitals to administration.<sup>15</sup>

Many healthcare systems globally are experiencing growing demand and increasing pressure on finite budgets. We believe delivering better patient care outcomes will reduce the burden on health systems, driving greater adoption of innovative care solutions. Through life-changing care, we focus on solutions that improve efficiency of care delivery, care provision outside of traditional care settings (such as in the home) and medical devices.

Improving efficiency of care delivery has significant potential to improve the patient experience, particularly given the slow adoption of technology in healthcare, a sector which is still reliant on fax machines.<sup>16</sup> Delivering care outside traditional care settings includes performing surgeries in outpatient clinics that used to require a hospital stay. Medical devices include wearable technology that can monitor patients continuously and alert caregivers if their condition deteriorates.

<sup>1</sup> World Health Organization – Tracking Universal Health Coverage: 2023 global monitoring report

<sup>14</sup> <https://ascopost.com/issues/june-10-2023/pembrolizumab-added-to-chemotherapy-improves-survival-in-advanced-cervical-cancer-regardless-of-pd-l1-expression/>; accessed on 03/11/2023

<sup>15</sup> <https://www.cms.gov/data-research/statistics-trends-and-reports/national-health-expenditure-data/projected>

<sup>16</sup> [www.statnews.com/2022/01/20/medicine-fax-machines-vital-technology/](https://www.statnews.com/2022/01/20/medicine-fax-machines-vital-technology/); accessed on 06/09/2023



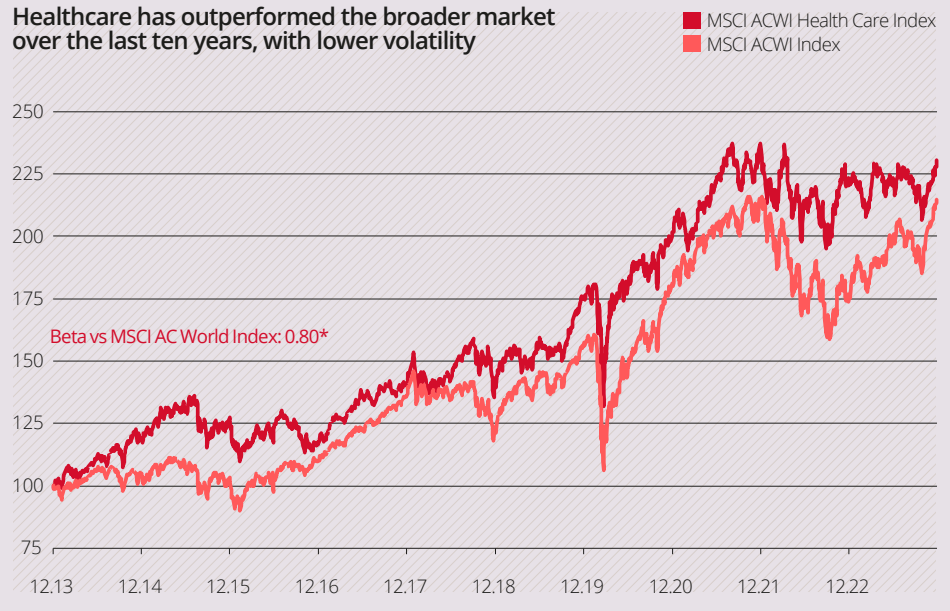
## Why invest now?

We are at a pivotal moment in global health. Non-communicable diseases, such as cardiovascular disease, account for 41 million deaths globally per year and the UN has issued a global action plan to cut the number of deaths by one-third by 2030.<sup>17</sup> At the same time, many health systems globally remain disrupted in the wake of the COVID-19 pandemic.<sup>18</sup> We believe investors can capitalise on the increased focus on global health and innovation catalysed by the COVID-19 pandemic, and focusing on what matters to patients gives a higher probability of success.

We believe the healthcare sector typically displays less demand volatility than other sectors due to the less discretionary nature of healthcare consumption. Investing in healthcare therefore has the potential to exhibit lower cyclical volatility, while still focusing on growth. By targeting life-changing treatments, investors can gain exposure to companies who are likely well-placed to succeed given the greater value placed on these treatments by patients.

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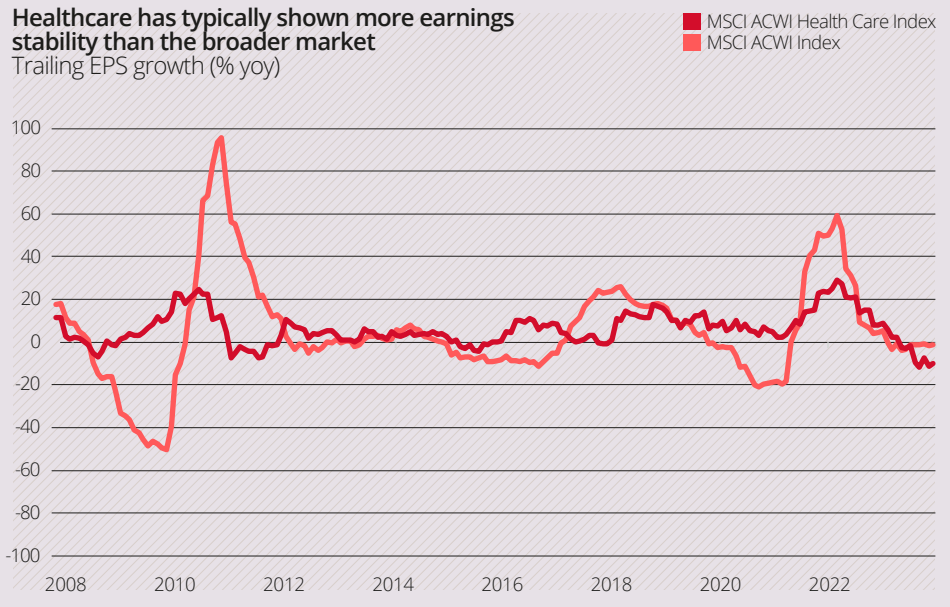
### Healthcare has outperformed the broader market over the last ten years, with lower volatility



Source: Bloomberg, total returns as at 31 December 2023, \*calculated weekly. Past performance is not a guide to the future. No investment strategy or risk management technique can guarantee returns or eliminate risks in any market environment.

### Healthcare has typically shown more earnings stability than the broader market

Trailing EPS growth (% yoy)



Source: Factset, Redwheel. From 2008-2023 – captures the Great Recession. Past performance is not a guide to the future. No investment strategy or risk management technique can guarantee returns or eliminate risks in any market environment.

Focusing on life-changing treatments offers themes specifically focused on the social pillar of ESG and, therefore, may offer diversification benefits alongside environment-focused thematic investment strategies for investors looking for responsible investment solutions. This clear alignment with the social pillar of ESG is due to the more active role a strategy focused on life-changing treatments can take in tackling social issues such as unequal access to care, global vaccination initiatives and infant mortality.

<sup>17</sup> <https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases>

<sup>18</sup> <https://www.who.int/europe/news/item/20-07-2022-covid-19-has-caused-major-disruptions-and-backlogs-in-health-care-new-who-study-finds> accessed on 23/08/2023

**Maximising impact through a patients-first focus**

- Focusing on what matters most to patients through investing in companies providing life-changing solutions helps us direct capital towards those solutions that should have a greater positive impact on society.
- Considering the implications of companies' decisions on patient access further enhances the impact on patients and society, which should also lead to better commercial outcomes.
- For example, over 500 million people worldwide have diabetes and it is estimated that this figure will grow to 1.3 billion by 2050.<sup>19</sup>
  - Our strategy is exposed to various diabetes solutions, including continuous glucose monitors (CGMs) that have revolutionised patient care and allow patients to measure their glucose levels less invasively and in real time.
  - Dexcom and Abbott, for example, are leading producers of CGMs. The former's latest CGMs, Dexcom G6 and G7, leverage precision and useful features such as automatic glucose readings to attract demand, the latter's, Freestyle Libre 2 and 3, leverage affordability.

The Redwheel Life Changing Treatments Strategy seeks investments in companies delivering healthcare solutions that improve patients' lives, regardless of where they live and without sacrificing investor returns. The strategy leverages the team's healthcare investment expertise and scientific backgrounds to invest globally and across the market capitalisation spectrum in long-term sustainable growth opportunities within the healthcare space. We look for those companies that play into the three aforementioned themes we believe will have the greatest positive impact on patients' lives, which should also lead to better commercial outcomes.

<sup>19</sup> <https://www.thelancet.com/series/global-inequity-diabetes> accessed on 4/8/2023

## Key Information

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