Morgan Stanley

INVESTMENT MANAGEMENT

Global Equity Observer

Diagnostics: The Workhorse of Improving Health Outcomes

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For health care companies, the holy grail of compounding at high returns is underpinned by pricing power, barriers to entry and non-discretionary end market demand. Whilst non-discretionary demand can provide a ballast to compounding power for investors, it has stark implications for other stakeholders: for the patient, it may mean "no other choice". "Non-discretionary" often means overburdened health systems—because hospitals and providers cannot cut back on treatment when budgets tighten, costs balloon or patient numbers increase.

This forces the question: what constitutes a valuable health care intervention? We think that wider use of diagnostic testing and early screening carries the benefit of improved patient outcomes, as well as the potential to optimise health care expenditure. Diagnostics inform 70% of clinical decisions, yet comprise only 2% to 5% of health care funding.¹

Reducing the Cost of Sickness

It was refreshing to see the chairman of the UK-based biopharmaceutical business we own talk about the need to "reduce the cost of sickness" at the 2023 World Economic Forum in Davos earlier this year.² During his address, Mr.

AUTHOR



HELENA MILES Vice President, Research Analyst

"Together, diagnostics and predictive analytics can enable clinicians to make better treatment decisions and even keep patients out of hospital."

¹Source: Roche Diagram, "Breaking Silos to Unlock the Value of Diagnostics", Edition 2017, Volume 2.

² Source: BBC News, "Technology can help the NHS, says AstraZeneca boss", 23 January 2023.

Johansson was clear that achievement of this goal lies in screening and early diagnosis, rather than in drug development alone. This is an interesting comment coming from the chairman of one of the world's largest drug developers; but perhaps a warranted one given the extraordinary spending by pharmaceutical companies on research and development (R&D). Annual oncology R&D spend is estimated to be around US\$50 billion globally,³ but improvement of survival rates has been stubbornly slow. Interventions being developed by large pharmaceutical companies generally target advanced disease, with drugs extending median survival by months not years. In the 30 years between 1992 and 2022, survival rates for American women with late-stage breast cancer doubled, but only to 29%.⁴

The potential for diagnostics and early-stage screening to improve survival rates looks enormous. In the case of cancer, the earlier the disease is treated, the more likely that pharmaceutical interventions will extend survival. Take the example of breast cancer: the five-year survival rate for women in the U.S. with breast cancer that has not spread beyond the breast is 99%. ^{5.6} However, if the cancer has spread, the survival rate falls dramatically, to just 29%. The difference between the two survival rates is down to when the disease is caught and diagnosed.

Together, diagnostics and predictive analytics can enable clinicians to make better treatment decisions and even keep patients out of hospital. Predictive algorithms have been used in intensive care units to identify patients more likely to need surgical interventions. Hospitals have reported reduction in mortality as a result. On top of this, 39% of surveyed health care executives said that using predictive analytics and diagnostics had reduced costs.

The cost reduction to the health care system from wider use of diagnostics and screening can be significant. For example, it is estimated that the cost of treating a specific type of lung cancer is \$231,000 per year in the U.S.9 Compare this to an equivalent screening cost of \$19,000 per year, or less than 10% of the cost of treatment. Additionally, if physicians can correctly

identify the type of disease through diagnostic testing, health care systems do not waste costly drugs on patients whose cancer would not have responded to that drug in the first place. As such, specific diagnostic testing may also enable physicians to provide more cost-effective treatment.

Striking the Right Balance

Of course, there has to be a balance struck between improving current levels of screening and not overburdening health systems with the cost of screening entire populations too frequently. Screening whole populations for lung cancer at \$19,000 per year is not exactly an insignificant financial burden. There is also the issue of false positives for populations who are over-screened or are sent for screening when the disease would be too small to detect anyway. Possibly the best example of early-stage screening is also the oldest: the Pap smear (testing for cervical cancer) only entered widespread use 40 years after its invention, in the 1960s. Since then, incidence and mortality rates for cervical cancer have come down by more than 50%. Despite this success, it took 40 years to fully implement a screening programme. This shows that balancing cost, precision and behavioural adaptations is not easy.

There is also the question of those diseases for which screening is available but therapeutic intervention is currently limited. A pertinent case of this is screening for the genetic risk of developing Alzheimer's disease. Australian actor Chris Hemsworth recently revealed that he is at increased risk of developing Alzheimer's after he underwent genetic testing. He was found to be a carrier of a gene that increases his risk of developing the disease eight to 12-fold versus someone who does not carry a copy of the gene at all.¹² Although this information can be helpful in terms of managing risk factors, not everyone may have the ability to employ interventions to manage the risk (such as exercise, diet or experimental therapies). The test can tell a patient if they are at heightened genetic risk of developing Alzheimer's but does not offer a treatment. Whilst this certainly holds advantages, it can raise more questions than answers on an ethical front. As such, there is clearly a balancing act between diagnosis/screening and therapeutic interventions.

³ Source: McKinsey, Our Insights: "Pursuing breakthroughs in cancer-drug development". Published January 12, 2018.

^{*}Source: Angela B. Mariotto, Ruth Etzoni, Marc Hurlbert, Lynne Penberthy and Musa Mayer, "Estimation of the Number of Women Living with Metastatic Breast Cancer in the United States", Cancer epidemiology, biomarkers & prevention: a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. Published online 18 May 2017. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5833304/

⁵ Source: cancer.net "Breast Cancer: Statistics". Statistics adapted from the American Cancer Society's publications, "Cancer Facts & Figures 2023" and "Cancer Facts & Figures 2020"; the International Agency for Research on Cancer website; and the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program. All sources accessed February 2023.

⁶ Five-year survival rate = percentage of patients still alive within five years of the cancer being detected

⁷ Source: philips.com "Predictive analytics in healthcare: three real-world examples", 12 June 2020.

⁸ Source: philips.co.uk "Early Warning Score reduces incidence of serious events in general ward"

⁹ Source: siemens-healthineers.com "Lung cancer screening: A lever to reduce cancer mortality"

 $^{^{\}rm 10}$ Source: siemens-healthineers.com "Lung cancer screening: A lever to reduce cancer mortality"

¹¹ Source: cancer.org "History of Cancer Screening and Early Detection: 20th Century to Present", last revised 17 May 2021. https://www.cancer.org/treatment/understanding-your-diagnosis/history-of-cancer/screening-early-detection.html

¹² Source: National Institute on Aging, "Study reveals how APOE4 gene may increase risk for dementia", 16 March 2021, available at nia.nih.gov.

Diagnostics companies are exposed to massively important trends in the improvement of health outcomes and the need for providers to manage costs. They often enjoy high levels of recurring revenues and barriers to entry: once a diagnostic machine is installed, the manufacturer will sell consumables that allow the machine to run different diagnostic tests. This often ensures a captive customer for high margin and predictable revenue streams. We think that these features make diagnostics businesses high quality companies to invest in.

We own several diagnostics companies in our global portfolios. Our life sciences holdings derive between one-quarter and one-third of their revenues from diagnostic testing. They hold large market shares in a concentrated and growing end market. Innovation from these companies has enabled improvement in the quality, breadth and efficiency of diagnostic testing. For example, the American multinational medical devices and health care company we own is developing a blood test that can test for concussion and predict outcomes from brain injuries within 15 minutes.¹³

Another customer for diagnostic testing is the pharmaceutical and biotech industry. In many cases, diagnostics providers are also important to the drug development process, through their manufacture of "companion diagnostics". Diagnostic tests will often be developed alongside a drug to better identify

patients who should have a positive response to it. For example, the American analytical instruments provider we own is partnering with the biopharmaceutical business we hold to develop diagnostic tests for some of its oncology drugs. For the analytical instruments provider, this carries the benefit of resilient end market demand and regulatory protection, without the risks associated with traditional pharmaceutical company revenues: trial failures, patent expiries and pricing pressures.

Conclusion

Having seen the potential for diagnostic testing and early-stage screening to reduce the cost of sickness, it feels fair to argue that this should be viewed as a non-discretionary, if not under-used, cog in the health care ecosystem. We think that demand for diagnostics is well underpinned given that the use case for wider and early-stage screening is strong.

For the investor, these companies can offer high returns on operating capital employed, underpinned by barriers to entry and recurring revenues. They are exposed to massively important trends where they can enable better outcomes and save on costs. We rarely see these companies dominate the headlines for major advances in curative therapies, but beneath the surface they have strong potential to meaningfully improve mortality rates from life-limiting diseases.

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There is no assurance that a portfolio will achieve its investment objective. Portfolios are subject to market risk, which is the possibility that the market value of securities owned by the portfolio will decline. Market values can change daily due to economic and other events (e.g. natural disasters, health crises, terrorism, conflicts and social unrest) that affect markets, countries, companies or governments. It is difficult to predict the timing, duration, and potential adverse effects (e.g. portfolio liquidity) of events. Accordingly, you can lose money investing in this strategy. Please be aware that this strategy may be subject to certain additional risks. Changes in the worldwide economy, consumer spending, competition, demographics and consumer preferences, government regulation and economic conditions may adversely affect global franchise companies and may negatively impact the strategy to a greater extent than if the strategy's assets were invested in a wider variety of companies. In general, equity securities' values also fluctuate in response to activities specific to a company. Investments in foreign markets entail special risks such as currency, political, economic, and market risks. Stocks of small- and mid-capitalisation companies carry special risks, such as limited product lines, markets and financial resources, and greater market volatility than securities of larger, more established companies. The risks of investing in emerging market countries are greater than risks associated with investments in foreign developed markets. Derivative instruments may disproportionately increase losses and have a significant impact on performance. They also may be subject to counterparty, liquidity, valuation, correlation and market risks. Illiquid securities may be more difficult to sell and value than publicly traded securities (liquidity risk). Non-diversified portfolios often invest in a more limited number of issuers. As such, changes in the financial condition or market value of a single issuer may cause greater volatility. **ESG strategies** that incorporate impact investing and/or Environmental, Social and Governance (ESG) factors could result in relative investment performance deviating from other strategies or broad market benchmarks, depending on whether such sectors or investments are in or out of favor in the market. As a result, there is no assurance ESG strategies could result in more favorable investment performance.

¹³ Source: Abbott, "New Study Shows Abbott's Blood Test for Concussion Could Predict Outcomes From Brain Injury and Inform Treatment Interventions", 11 August 2022, press release.

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