



Regnan Global Equity Impact Solutions Strategy

Quarterly Impact Report

Q4 2021

Brought to you by J O Hambro Capital Management

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With hindsight, looking back at the last quarter of 2021, it now looks a lot like “the calm before the storm”. And that is in spite of a bout of volatility that was sparked by fears of the Omicron variant of COVID-19 into the last month of the year.

Those fears proved fleeting, as it became increasingly apparent that Omicron, while more transmissible, was less virulent, meaning that the disruption it imposed on the global economy would ultimately turn out to be shorter-lived than preceding variants.

2021 was billed as a year of recovery. Following the remarkable year that was 2020, 2021 was to see some return to some sort of normalcy ushered back in, however relapse waves of COVID and different government reactions to them around the world meant that what materialized was a staggered and uneven recovery, from region to region.

This, combined with rampant commodity inflation and supply chain shortages, made for a year where volatility was rife, and sentiment shifted vigorously over the course of the year.

One thing that was also evident as countries across the globe struggled to emerge from the hold of the pandemic is that our healthcare systems need to evolve. If we are to deal with future pandemics and other new threats, on top of existing challenges – such as rising heart disease, cancer rates, obesity, just to name a few – we need to evolve our healthcare systems to make better use of already stretched resources.

As an example, portfolio holding Novo Nordisk has presented physicians with a new and effective therapy for clinical obesity, Wegovy – a treatment launched in the second half of last year. For the first time ever, morbidly obese patients have an alternative to surgery that is safer and cheaper than resorting straight to bariatric surgery.

Big structural shifts are afoot in the healthcare space, particularly with a new generation of biological therapies launching, which are based on monoclonal antibodies enabled by the likes of Abcam, Sartorius Stedim Biotech and contract manufacturers like Lonza – all of which are also held by the strategy. And the future looks even brighter if the biotech research and development that these companies facilitate are also successful in using their platforms to scale up ground-breaking cell and gene therapies.

Beyond therapy however, we also need to ask whether the healthcare model we all are so used to, where we discover an ailment, have it diagnosed and are prescribed treatment, is still fit for purpose in today’s increasingly resource-constrained world.

Read on to learn more about liquid biopsy – this is just one emerging diagnostics innovation that, along with more mature technologies like next-generation gene sequencing and PCR, can enable a transition towards a more proactive and preventative healthcare model, where ailments such as cancers may one day be caught through regular broad-based screening tests, rather than invasive biopsies that target a specific pathogen.

Qiagen, one of the two names featured in this quarter’s report, will be a key enabler for the preparation of liquid biopsy samples, in this exciting new segment of the molecular diagnostics industry that is critical to achieving multiple SDG 3 targets.

The other featured portfolio holding this quarter is Dürr, a Stuttgart-based engineering business that specializes in automating manufacturing processes using robotics combined with automation technology that can drastically reduce the material footprint for their industrial customers – a contribution to SDG 12 that is also increasingly relevant in an inflationary world, where customers have a bigger financial incentive than ever to cut their bill of materials!



Tim Crockford,
Senior Fund Manager, Head of Equity Impact Solutions
Regnan Global Equity Impact Solutions



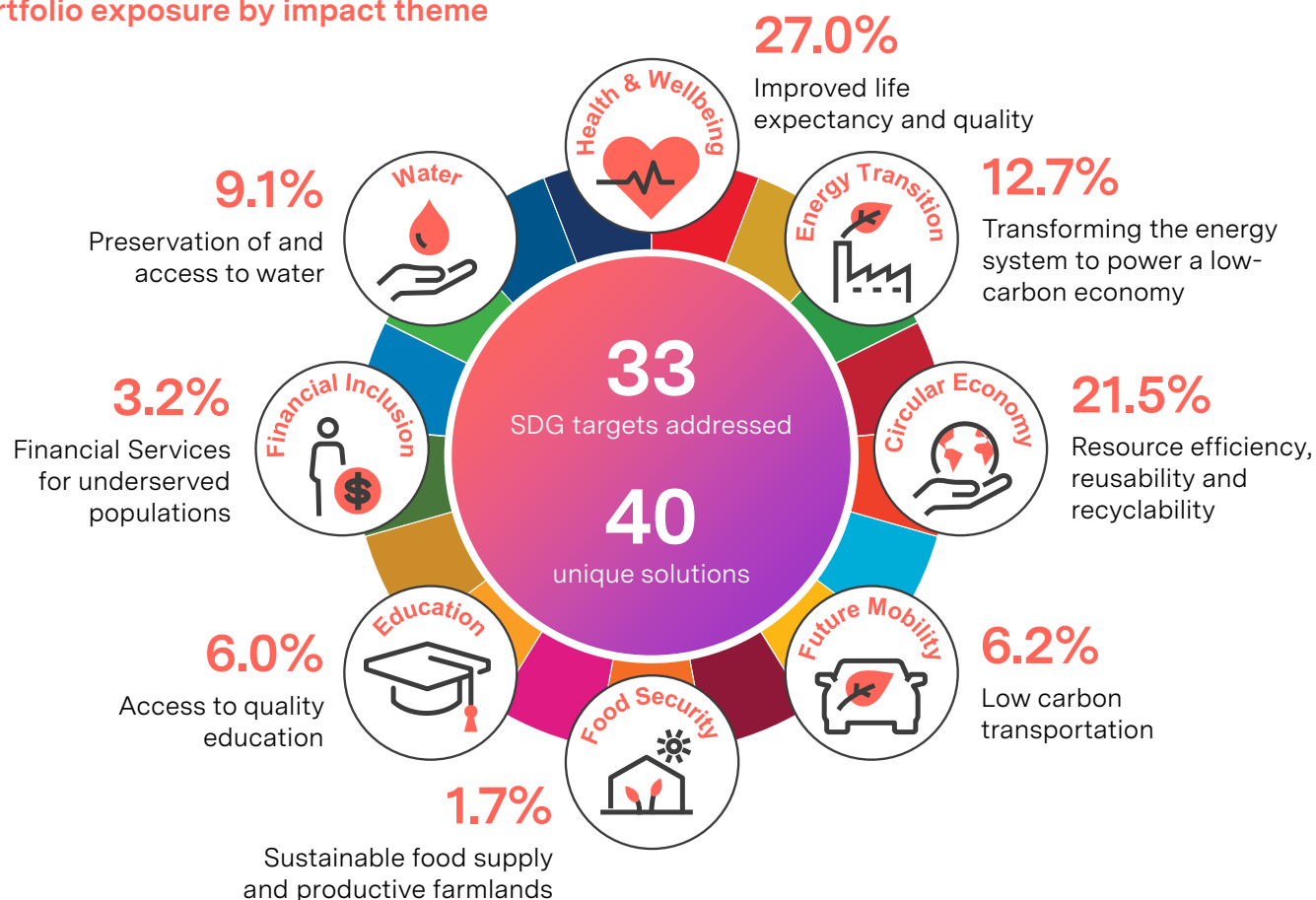
The Regnan Global Equity Impact Solutions strategy is a solutions-first strategy. It is focused on investing in mission-driven businesses that address underserved environmental and social challenges and deliver real, systematic change for the better. The team aspires to demonstrate that investing for impact not only makes good environmental and social sense; it also makes good financial sense. The intention is to broaden the appeal of impact investing and redirect capital towards impact investing. We aim to do this by delivering our investors market-beating long-term returns because we have identified 'system changers' that innovate, disrupt and ultimately produce positive environmental, social and financial outcomes.

Strategy Overview

- The strategy aims to generate long-term outperformance by investing in the listed shares of mission-driven companies that create value for investors by providing solutions for the growing unmet sustainability needs of society and the environment, using the United Nations Sustainable Development Goals (SDGs) as an investment lens.
- Underpinned by the Regnan SDG taxonomy – the team has built a comprehensive proprietary framework to identify companies that provide solutions to the environmental and societal challenges facing the world.
- An actively managed, high conviction, diversified, global multi-cap portfolio with very low portfolio turnover and a strong emphasis on driving impact through engagement.
- Benchmark: MSCI ACWI Investable Market Index.
- The use of the Index does not limit the investment decisions of the fund manager, therefore the composition of the portfolio may differ significantly from those of the Index.

Regnan Global Equity Impact Solutions

Portfolio exposure by impact theme



Source: Regnan / JOHCM as of December 31, 2021. Note: Thematic exposure attribution to eight impact themes based on estimates of company revenues or other relevant metrics. Cash position: 2.1%. Neutral impact (12.1%) is estimated where revenues not directly tied to any theme. Negative impact (2.2%) estimated where revenues may be detrimental to UN Sustainable Development Goals (SDG). Data representative of Regnan Global Equity Impact Solutions Fund (U.K.) onshore OEIC.

Liquid Biopsy: Flesh or blood?

A brief description

At its root, liquid biopsy is an *in vitro* diagnostic test, a test that takes place outside of a living organism, for example in a test tube or culture dish. *In vitro* tests are indispensable, informing approximately 70% of clinical decision-making. Liquid biopsies diagnose disease by identifying relevant biomarkers within liquids.

¹CDC. <https://www.cdc.gov/csels/dls/strengthening-clinical-labs.html>

A disruptive promise

Liquid biopsy aims to displace the current diagnostic paradigm in biopsy: tissue-based biopsy. Liquid biopsy has three critical advantages over its tissue-based counterpart.

1. Liquid biopsies are non-invasive, while tissue biopsies are an invasive, and at times risky procedures, especially when the tumor/disease site is difficult to access.
2. Liquid biopsies generate a complete genetic profile of the tumor/disease and are not limited by regional heterogeneity.
3. Liquid biopsies enable repeat testing at fast turnaround times, which is critical for determining treatment efficacy and tumor/disease evolution.

A promising solution for cancer diagnosis

Although it can be used for other applications, the excitement around liquid biopsy springs from its potential to diagnose cancer. Cancer remains one of the world's deadliest and fastest growing diseases. According to the World Health Organization (WHO), cancer is responsible for 1 in 6 deaths worldwide, 70% of which occur in low-to middle-income countries.

Cancer diagnosis and treatment remains an immense challenge due to the disease's insidious, shapeshifting quality. Liquid biopsy could prove a revolutionary diagnostic weapon against cancer due to its potential to monitor disease progression in real-time, allowing clinicians to rapidly adapt the treatment in response to the quickly-evolving cancer.

Cancer 'invades' the body through the bloodstream, via a process called metastasis. As they metastasize, most solid cancers shed either entire cells, or fragments of cells into said bloodstream. Both cells and cellular fragments are biomarkers which liquid biopsies aim to detect.

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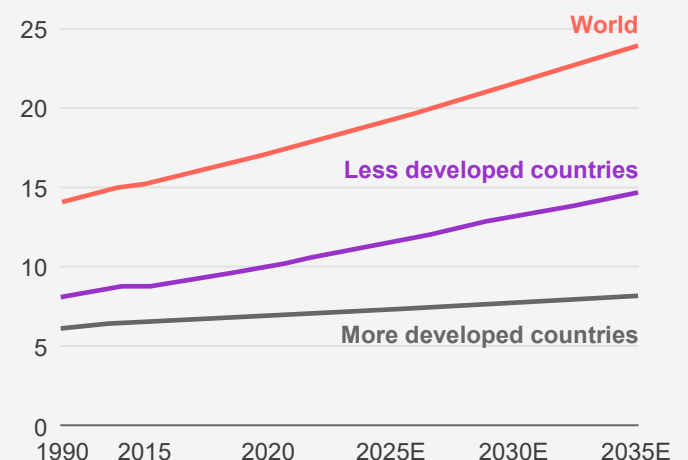
“Cancer is an expansionist disease; it invades through tissues, sets up colonies in hostile landscapes, seeking “sanctuary” in one organ and then immigrating to another. It lives desperately, inventively, fiercely, territorially, cannily, and defensively—at times, as if teaching us how to survive. To confront cancer is to encounter a parallel species, one perhaps more adapted to survival than even we are.”

Source: Siddhartha Mukherjee, *The Emperor of All Maladies*

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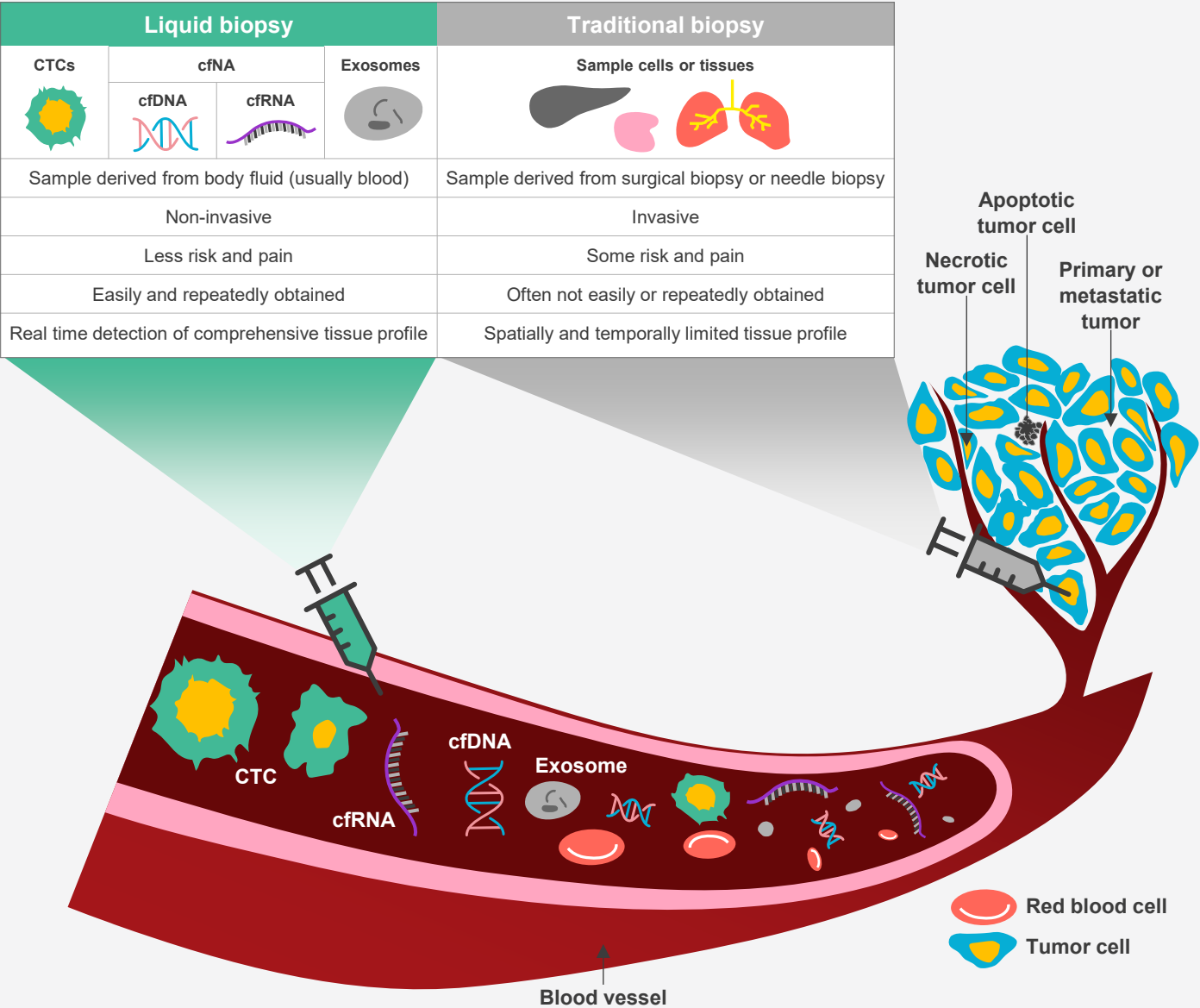
Predicted global cancer cases, 2012–2035

Cases (millions)



Source: WHO GloboCan, BBC.

Liquid biopsy vs. traditional biopsy



Source: researchgate.net

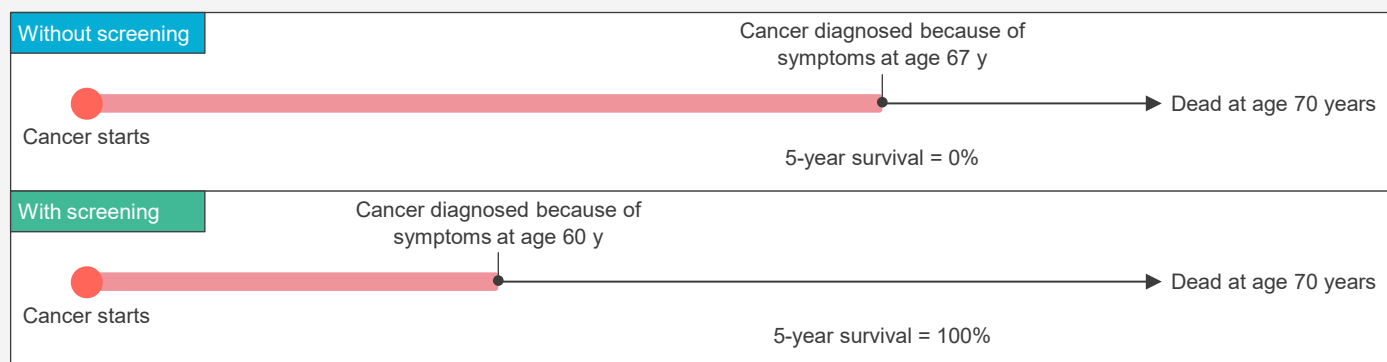
A multi-market opportunity

To put it simply, the size of the total addressable market depends on how early liquid biopsy can diagnose cancer. Earlier-stage cancers are easier to treat as they are more localized and are unlikely to have metastasized significantly beyond their place of origin.

However, early cancer detection is technically more difficult. Earlier-stage, localized cancers shed less genetic material into the bloodstream. This low volume of cancerous cells or cellular fragments results in a high signal-to-noise ratio, making detection more difficult.

The most established, yet the smallest market for liquid biopsy is therapy selection for late-stage cancers, followed by the less-established but bigger monitoring market. However, the excitement sparked by liquid biopsy based on its potential for early detection and screening of cancers. The majority of cancers today have no associated screening tests, and a number of companies are developing ‘pan-cancer’ screening tests which aim to detect over 50 types of cancer in a single blood sample.

Lead-time bias



Source: Wegwarth, O., Schwartz, L. M., Woloshin, S., Gaissmaier, W., & Gigerenzer, G. (2012). Do physicians understand cancer screening statistics? A national survey of primary care physicians in the United States. *Annals of internal medicine*, 156(5), 340-349.

A wealth of remaining challenges

Clinically useful outcomes

Earlier diagnosis is only useful if the diagnosed cancers can also be treated earlier. Even if liquid biopsy proves successful, treatment paradigms will need to evolve in order to make early detection of cancer clinically useful. A key hurdle to treatment of early-stage tumors is the identification of their location of origin, which remains a challenge within liquid biopsy.

Sensitivity and specificity

Sensitivity and specificity remain a challenge for this fledgling diagnostic tool. As illustrated previously, early-stage tumors only shed low concentrations of cancerous cells or fragments. Low sensitivity in detection results in false negatives, by not being able to detect these low concentrations. Low specificity in detection, on the other hand, leads to false positives, whereby the detected biomarkers do not lead to the patient developing the disease at a later stage.

Reimbursement

The pathway to financial reimbursement for diagnostic tests is complex and lengthy, particularly in the US. While liquid biopsies for later-stage cancers benefit from a better-established path, the reimbursement landscape for pan-cancer screening test is much more uncertain. The viability of pan-cancer screening, in terms of coverage from large payers, is likely to hinge on both legislative change and the industry's ability to drive cost reductions.

Summary

Liquid biopsy's promise is clear: a non-invasive means to identify and track the evolution of a disease, which in turn allows for continuous tweaking of the treatment regimen. This promise is particularly salient for cancer, a disease characterized by its shapeshifting quality, late-stage detection and more generally, limited diagnostic tests. Nevertheless, liquid biopsy has significant technical and reimbursement hurdles to overcome before it can realize its promise.

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QIAGEN

CASE STUDY

This company's activities contribute to the following
SDG targets and Regnan themes:



TARGET 3.2

TARGET 3.3

TARGET 3.4



Theory of Change

Despite influencing 70% of medical decisions, lab or diagnostic tests are estimated to only account for 2-5% of healthcare spending. While it is difficult to make general statements about how diagnostic tests improve healthcare outcomes, HIDA estimates that appropriate diagnostic test use could help to avoid \$900m of healthcare costs in the US alone. Molecular diagnostics is the fastest-growing segment of the in vitro diagnostics industry by virtue of enabling earlier diagnosis, allowing monitoring of disease progression and through offering better guidance for therapeutic decision-making. Qiagen's 'Sample to Insight' product philosophy is designed to facilitate uptake of molecular diagnostics. By empowering users without sophisticated expertise in molecular biology to use molecular diagnostic technologies, taking them straight from the biological sample to actionable insight, Qiagen expands the adoption of molecular diagnostics, and thus improves patient outcomes. We will seek to increase net positive impact at Qiagen through encouraging it to refine its materiality assessment, set ambitious, long-term targets for net impact improvements and lastly, oversee the company's leadership transition.

What they do

Founded in 1986, Qiagen's success is built upon its Sample to Insight solutions: the provision of molecular insights from biological samples. These solutions are in the form of proprietary sample and assay technology to extract, purify, amplify, and interpret DNA, RNA, and proteins. Qiagen serves more than 500,000 customers in two broad customer groups: Molecular Diagnostics (human healthcare) and Life Sciences (academia, pharma R&D and industrial applications, primarily forensics). The company estimates that its total addressable market (TAM) exceeds \$10 billion, with its c5000 employees serving customers in over 35 countries.

Why we own it

The dawn of precision medicine drives the need for innovative molecular diagnostics. While only accounting for c10% of the industry today, the molecular diagnostics market is expected to grow >10% p.a. in the coming years; growth will predominantly be propelled by its use beyond infectious diseases, which accounts for approximately half of the demand today.

Qiagen's Sample to Insight solutions portfolio, which includes several leading molecular diagnostics franchises, offer a differentiated, and defensive, way to gain exposure to this growth. The expansion of molecular diagnostics beyond infectious diseases, championed by Qiagen, for instance towards immune disorders and prenatal and neonatal health, is an important driver of its growth. Qiagen is also an impressively defensive business, with the majority of its sales coming from its more than 500 consumables and a diversified instruments exposure, with several leading franchises.

However, Qiagen's solutions not only expand applications of molecular diagnostics, but also push the boundaries of innovation. For instance, its proprietary development of QuantiFERON-TB, which has replaced a century-old skin prick test for diagnosing latent tuberculosis (TB). Last year, Qiagen launched a battery-operated version of this test for high-burden regions with limited laboratory infrastructure: the QIArearch QuantiFERON-TB test. The WHO has classified 30 countries in these regions as high-burden, representing an estimated 85% of the global TB burden. QIArearch had already been recognized as a significant health innovation by the Joint United Nations Program on HIV/AIDS (UNAIDS), even before its commercial launch. QIArearch is just one, albeit transformative, example of how Qiagen democratizes diagnostic testing.

99%

of TB deaths occur in
developing countries

40%

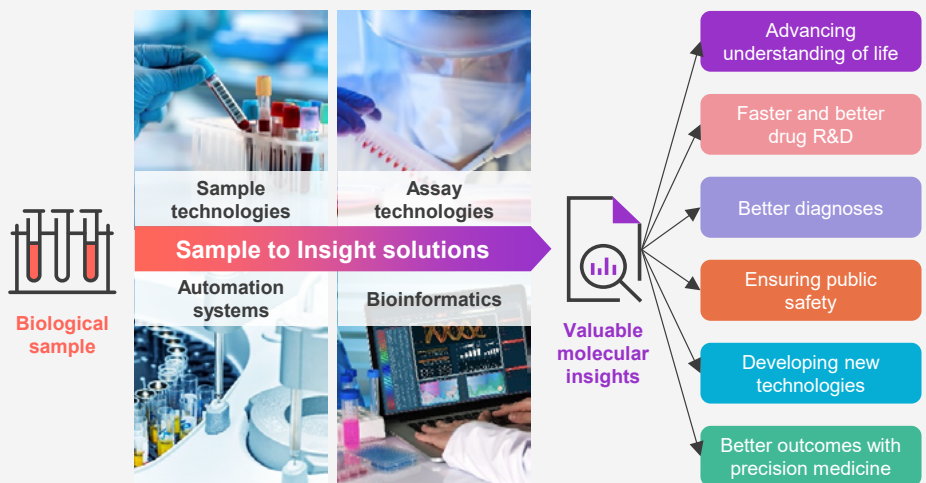
of cases are undiagnosed
or not reported

1 USD

in TB prevention returns

40 USD

in economic benefits





DUERR

CASE STUDY

This company's activities contribute to the following SDG targets and Regnan themes:

TARGET 7.3



TARGET 8.4



TARGET 9.4



Theory of Change

Duerr provides solutions to automotive and other industrial customers to improve resource efficiency in production, thereby contributing towards a circular system. Duerr creates a positive impact through its products and services by supporting electric vehicle production and subsequent carbon emission reductions, as well as by reducing the amount of materials wastage by their customers. Duerr's robotic assembly lines improve the ramp-up of EV production through helping OEMs, including new entrants, to rapidly scale EV production and to provide high-voltage end of line testing. Duerr is also involved along the battery production value chain, specifically around coating electrodes as well as assembling the battery pack with its innovative gluing application technology which has important safety features when it comes to crash safety. Paint application is very energy intensive, Duerr has innovated to significantly reduce the environmental impact of paint shops over the past decade with a 67% reduction in energy, 71% reduction in water, 73% reduction in VOC and 36% reduction in paint use.

What they do

Duerr is one of the world's leading mechanical and plant engineering firms with extensive expertise in automation and digitalization/Industry 4.0. Its products, systems and services enable highly efficient and resource-saving manufacturing processes in different industries. The automotive industry is the largest end market (c50% revenues), Duerr plans and builds paint shops for the car industry, as well as robot-based solutions for the automated application of paint. It also engages in balancing, cleaning, wood-processing machines, and air purification systems. It operates five divisions: Paint and Assembly Systems, Application Technology, Measuring and Process Systems, Wood Processing Systems (Homag), and Clean Technology Systems.

Why we own it

Duerr develops products and provides solutions that facilitate low-consumption and low-emission processes that can reduce the environmental footprint of factories across of a broad range of growing end markets. Duerr is global market leader in about 95% of its product portfolio, with high barriers to entry and dominant market shares.

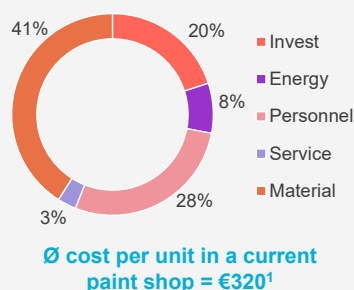
Paint application is extremely energy and water intensive. Approximately 70% of total energy consumption at an automotive assembly facility takes place in the paint shop. Duerr has innovated to significantly reduce the environmental impact of paint shops over the past decade with a 67% reduction in energy, 71% reduction in water, 73% reduction in volatile organic compounds (VOC) and 36% reduction in paint use. Through a collaboration with PPG, Duerr has recently developed a new paint process that can reduce energy consumption by up to 39% (vs 2018 levels) by significantly lower curing temperatures, and enabling faster flash and dehydration times.

Duerr acquired Homag in 2014, which took the business into wood working machinery and systems, with a strong focus on digital solutions. Homag's intelliDivide software generates optimized cutting patterns, which helps its customers to reduce waste, decrease material consumption (by up to 10%) and leads to more efficient production processes. Sustainability is a key driver for Homag, through its timber frame house building business (Weinmann), Duerr is contributing towards reducing CO2 emissions by 90% compared to traditional construction methods.

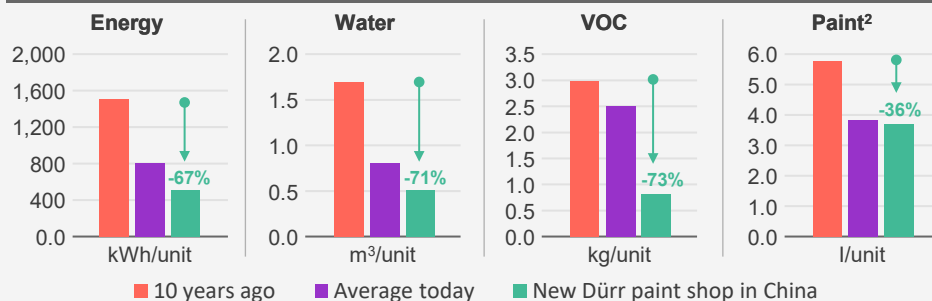
Within Clean Technology Systems, exhaust air purification systems remain key for industrial customers to meet regulatory requirements. Duerr's Organic Rankine Cycles (ORC) system is one of the most important products in this division, the system generates electricity from waste heat emitted from manufacturing plants, allowing plants to produce their own electricity while reducing their carbon footprint.

Innovation: R&D efforts focused on tangible customer value

Cost per unit in a paint shop



Reduction of resource consumption/emissions in paint shops of a German OEM



Source: Duerr AG, CCI, Investor Relations Presentation, Bietigheim-Bissingen, March 2018. ¹Compared to €420 15 years ago. ²In spray booth only.

About Regnan

At Regnan we've been thinking forward and shaping the responsible investment movement since 1996 – long before it became mainstream.

2020 marked our expansion into funds management supported by the investment platform of J O Hambro and the Pandal Group. We've brought together proven sustainability and impact teams with track records tested through cycle, with the depth of insights provided by our engagement, advisory and research team.

Our collective purpose is to contribute to a more sustainable future by developing and promoting principled, rigorous and outcome-oriented approaches in responsible investment.

Client solutions sit at the heart of all that we do and are based on four key pillars:

- Delivering our clients attractive investment returns; we aim to grow their real wealth over the long term.
- Understand the materiality of sustainability issues to deliver improve decision-making and real world outcomes.
- Creating differentiated, innovative strategies that serve a purpose in client portfolios.
- Our strategies are authentic and provide significant exposure to underlying sustainability opportunities.

Regnan Global Equity Impact Solutions

The Regnan Global Equity Impact Solutions strategy is a solutions-first approach, focused on investing in mission-driven businesses that address underserved environmental and social challenges and deliver real, systematic change for the better. It is a high-conviction, global, multi-capitalization portfolio with low turnover and a strong emphasis on driving impact by engaging companies to improve measurable outcomes.

Regnan Sustainable Water and Waste

Our Thematic Investing team joined Regnan in April 2021 and launched the Regnan Sustainable Water and Waste Strategy in September 2021. Combining exposure to both water and waste-related companies makes this strategy a distinctive thematic investment proposition with diversification benefits.



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