CANDRIAM
A NEW YORK LIFE INVESTMENTS COMPANY

Innovation at the heart of oncology

World Cancer Day

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Marketing communication

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Cancer death rates have been falling over the past two decades, driven down by progress in cancer treatments, diagnosis tools and prevention strategies. Cutting-edge research and oncology technology innovations are transforming the industry, and more importantly patients' lives, as cancer survivors grow in numbers.

The evolution of cancer and the need for precision oncology

Starting from chemotherapy killing both healthy/normal and cancer cells without specificity, the field of oncology has moved towards targeted therapies. These therapies aim to reach cancer cells while sparing the healthy ones, thus increasing the success rate, and minimizing side effects. Over the years, many targeted therapeutics have been added to the arsenal of cancer treatment.

The use of Artificial Intelligence (AI), molecular modeling and other tools is expected to accelerate the pace of drug development, bringing new drugs to market in a timely fashion. Precision oncology and focused translational research efforts could help design better drugs, saving and prolonging patients' life.

A growing and competitive market

With ever-growing scientific knowledge of how cancer cells function, there is a tremendous amount of drug candidates that can potentially improve the standards of care in the near future. The number of clinical trials initiations in oncology has roughly doubled in the last 10 years[1]. The progress in clinical trials generates tens of unique new treatments approved each year, so in the battle against cancer, we are already equipped with many efficacious medicines, which clearly translate into improved benefits for patients.

1 - Global Oncology Trends 2022 Institute Report, IQVIA, https://www.iqvia.com/insights/the-iqvia-institute/reports/global-oncology-trends-2022

> **The number of clinical trials initiations in oncology has roughly doubled in the last 10 years[1].**

In multiple myeloma for example, which is the second most common hematologic cancer after lymphoma, drug development has led to impactful clinical outcomes. For decades, the only therapeutic option was chemotherapy. With 3 modern drugs approved around the beginning of the century, the therapeutic landscape has evolved to 15 currently available therapies, 12 of which were launched over the last 10 years. The availability of new, efficacious treatment regimens used sequentially and in combinations has translated to better survival of the patients: the relative 5-year survival rate had doubled over the last 20 years, now exceeding 60%. It is projected that patients could have gained almost 3 additional years of life as compared to 10 years ago[2].

For lung cancer, over 30 new drugs were launched during the last decade. Those drugs are mostly targeted therapies for a whole variety of cancer drivers, or they stimulate the immune system to better detect and kill cancer cells. Over the last 3 years the usage of non-selective chemotherapy has been the fastest-shrinking treatment option, replaced by targeted therapies and combinations of immunotherapies leading to increased survival[3]. In the future, we expect this positive trend in other cancer types as well.

These are two examples among many others; the number of breakthroughs in oncology has been increasing at a high pace in the last two decades.

Innovation: prepping for the future of drug development

In the illustration, we describe several modalities covering key aspects of drug development such as precision of the targeting, molecular selectivity, and new technologies. We believe that the next wave of therapeutics will include 1. protein degraders, whose goal is to trigger the complete degradation of oncogenic proteins (the proteins that have a potential to cause cancer); 2. synthetic lethality, an interesting concept where two or more different proteins interact to drive oncogenesis (i.e. the development of tumours); 3. antibody drug conjugates (ADCs)[4], and 4. small molecule inhibitors.

2 - National Cancer Institute - Surveillance, Epidemiology, and End Results Program, Cancer Stat Facts: Myeloma (https://seer.cancer.gov/statfacts/html/mulmy.html) and Impact of Novel Therapies on Multiple Myeloma Survival– Current and Future Outcomes - DOI:https://doi.org/10.1016/j.clml.2015.07.206
3 - as reported by IQVIA, a provider of analytics, technology solutions and clinical research services to the life sciences industry.
4 - ADCs are a class of biopharmaceutical drugs designed as a targeted therapy for treating cancer.

Antibody drug conjugates (ADCs) are well ahead of development, with currently 13 FDA-approved drugs, including some blockbusters, leading to more than $4B in sales and 17 business development deals in 2021[5]. In 2022 about 100 ADCs have been studied in clinical trials across 51 targets. A successful example is Daiichi-Sankyo's Enhertu, a game-changing therapy validating the company's platform. Turning the drug Herceptin into an antibody-drug conjugate has led to an unprecedented level of activity across several cancer types. In clinical trials, almost 90% of treated patients have experienced tumor shrinkage[6]. The drug has been so far approved for breast, gastric, and lung cancers and has generated global revenues of $426M in 2021[7], a little over a year after first approval. We see potential near-term impact on the entire sector with novel targets.

Illustration:
New therapeutic modalities in the fight against cancer

1 Precision	**Small molecules** Although small molecules have been used for decades, there is still room for innovation. Several generations of kinase inhibitors with increasing efficacy and safety.	**Protein degraders** New class of therapeutic solutions based on small molecules that allow not only to inhibit, but to eliminate the proteins responsible for various pathologies, previously considered undruggable.	**Synthetic Lethality** Exploiting interactions between gene pairs in cancer cells for therapeutic purposes inhibiting the product of one gene while the other one is mutated leads to cell death.
2 Selectivity	**Antibody drug conjugates** Designed to target disease-causing cells more effectively, without affecting healhy cells.	**Bispecific antibodies** Antibodies with two targets, e.g. T-cell activators, to push the natural immune system to fight the disease.	**Gene and cell therapies** Modifying the patient's genes to cure disease, increase the level of a missing enzyme, or repair a genetic defect.
3 New technology	**Liquid Biopsies** Non-invasive diagnostic technique that allows detecting cancer cells or their DNA circulating in the blood sample.	**AI** AI-assisted imaging - impressive accuracy and sensitivity of diagnosis	**RNA therapies** Modulating the expression of proteins, e.g., to reduce the levels of those causing a pathology.	**Exosomes** Cell-generated extracellular vesicles, which can be used as targeted drug delivery vehicles, potentially overcoming the challenges of systemic toxicity.

Source: Candriam

5 - ABC's of ADCs: Investor primer on antibody drug conjugates, Cowen, 2022
6 - Daiichi-Sankyo company presentations
7 - ADC Drugs Global Sales of 2021 and Future Prospects, https://www.biochempeg.com/article/261.html

Oncology, a highly dynamic segment in a resilient healthcare sector

The evolving need of discovering, funding, and developing new drugs makes the healthcare sector a highly resilient one within different macroeconomic environments. The sector also benefits from qualities such as high drug pricing, high margins, and significant clinical markets. The biotechnology revolution and favorable big pharma drug successes will continue and could play a meaningful role in the next decade. Oncology has seen some remarkable advances over the past few decades but we are just at the beginning of this incredible era. Cancer is a difficult and complex enemy, with multiple subtypes or histologies, and it is constantly changing in response to therapy. Today, doctors use a variety of treatments from chemotherapy to numerous increasingly sophisticated and highly efficacious targeted therapy options. With ever-growing scientific knowledge of how cancer cells function, there is a tremendous amount of drug candidates that can potentially improve the current standards of care in the near future. A record 30 oncology novel active substances (NASs) were initially launched globally in 2021, and a total of 159 have been launched over the last 10 years. As cancer is highly heterogeneous and always evolving disease, we need a wide variety of drugs used in combinations and in sequential treatment to help patients live better and longer lives. At Candriam, we research and seek to invest in the companies which are working on next-generation medicines that could save and prolong patients' life. Our dual experience in biotechnology as well as finance is a key advantage in identifying the game-changers.

While innovation is thriving, we focus on the most promising companies and drugs

As cancer is a highly heterogeneous and evolving disease, there is a need for multiple therapeutics to be used in combinations and in sequential treatments to increase clinical outcomes. The market of anti-cancer drugs is far from "one winner takes all" scenario, and it will always have room for successful contributors. Our experienced team at Candriam follows closely what is at stake in oncology drug development and seeks to invest in companies progressing drugs with a higher probability of success.

Rudi Van den Eynde

Head of Thematic Global Equity

Healthcare: a dynamic segment in the currently challenging macroeconomic environment

Healthcare stocks have held relatively well in the current macroeconomic and geopolitical landscape compared to the broad market. If the sector is not immune to inflation, high interest rates or economic slowdown, it was less impacted by these headwinds than many others. The evolving need of discovering, funding, and developing new drugs is combined with high drug pricing, high margins and significant clinical markets. Whilst inflation and input costs are an issue, manufacturing costs typically are not key to the pricing of medical products and drugs, the need to recover past R&D is a much bigger factor.

Major healthcare companies mostly have strong balance sheets lowly impacted by higher financing costs. Besides, consumption of medical products is not economically sensitive as diseases need to be treated regardless of economic conditions. Some subsectors such as medical technology are somewhat pressured by hospital staff shortages that may lead to lower current procedure numbers, which often turn out to be simply delayed. Investors remain cautious about the space and may prefer large pharma with solid business and commercial infrastructure. On the other hand, we have seen early-stage companies sealing very profitable deals with big pharma. We think this trend is vital to facilitate drug discovery, increasing appetite for new assets, M&A, and business consolidation.

Risks.

All our investment strategies involve risks, including the risk of loss of capital. The main risks associated with our Oncology strategy are:

- **ESG Investment Risk**

The non-financial objectives presented in this document are based upon the realization of assumptions made by Candriam. These assumptions are made according to Candriam's ESG rating models, the implementation of which necessitates access to various quantitative as well as qualitative data, depending on the sector and the exact activities of a given company. The availability, the quality and the reliability of these data can vary, and therefore can affect Candriam's ESG ratings. For more information on ESG investment risk, please refer to the prospectus of the fund.

- **Risk of capital loss**
- **Equity risk**
- **Currency risk**
- **Liquidity risk**
- **Concentration risk**
- **Derivative risk**
- **Emerging market risk**

€143 B

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