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Cancer Research: The March Continues with AI-powered Precision Oncology

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Cancer death rates have been falling over the past three decades[1], thanks to reductions in smoking, earlier detection, and improved treatment options in both the adjuvant and metastatic settings. However, incidence continues to increase for six of the top ten cancers including pancreatic and colorectal cancers. Innovations in translational research, clinical trial design and drug development are bringing new therapies to market and, more importantly, are transforming patients' lives, as cancer survivors grow in numbers.

1 - Source: www.cancer.gov/about-cancer/understanding/statistics#

Oncology research and treatment at the forefront of medical priorities worldwide

Cancer is a leading cause of death worldwide. According to the World Health Organization, prostate cancer, lung and bronchus (hereinafter lung) cancer, and colorectal cancer account for almost one half (48%) of all incident cases in men, with prostate cancer alone accounting for 29% of diagnoses. For women, breast, lung, and colorectal cancers account for 51% of all new diagnoses, with breast cancer alone accounting for 32% of cases. Among adults younger than 50 years, colorectal cancer is now the leading cause of cancer death in men and the second-leading cause in women (behind breast cancer), a rapid increase over the past 25 years – it ranked fourth in 1998. Additionally, cancer patients are shifting from older to middle-aged individuals who have many more years of life expectancy, and thus, opportunity to experience the late effects of treatment, including subsequent cancers – i.e. new primary cancers that occur in a person who has had cancer in the past.

Efforts to establishing molecular classification models for diagnosis and cures remain critical for bringing ad hoc prevention and treatment strategies.

The integration of artificial intelligence (AI) into medical innovation has had remarkable successes to date including immunotherapies and radiopharmaceuticals. However, we believe it is still at its infancy. For the future, we envision that personalised medicine will be integrated across multiple cancer indications and during the entire therapeutic journey of these patients, increasing our understanding of the disease and reducing its death toll.

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> **The potential benefits of precision oncology have yet to be fully realised. The use of next-generation DNA sequencing in metastatic cancer, the improvement toolkit for biomarker testing, and the use of artificial intelligence are key building blocks to develop more safe and effective treatments for each patient.**

Precision oncology, a new patient-centric approach to maximise clinical outcomes

In 2015, Barack Obama, President of the United States, launched the Precision Medicine Initiative to address the challenge of public health issues and diseases treatment, emphasising the need to deliver the right treatments, at the right time, every time to the right person.

Precision oncology is a form of personalised medicine applied to seek and treat defined histological and molecular variants of cancers with the aim of optimising patient screening and care, notably through the design of smart clinical trials[2]. This approach can improve treatment outcomes and transform lives by avoiding ineffective interventions – in addition to saving costs.

The discovery of biomarker-enriched strategies is a key innovation that shifted clinical trial design from conventional, costly large, single indication randomised controlled trials toward basket trials, which simultaneously evaluate treatments for multiple indications. These innovative trials also provide information that feeds AI tools to generate next generation drugs with a higher probability of maximising therapeutic responses for patients: this is called smart drug development.

Precision oncology is also key to identify the tumor intrinsic molecular characteristics that may be at the origin of recurrences after initial targeted therapy (tumor that come back, metastases). The idea is combining biological information with AI to collect genomic information as comprehensive as possible from relapse tumors, metastasised tumors and blood, to further analyse the change of tumor drivers. Eventually, all these efforts will bring new knowledge on how to tackle difficult to treat cancers with smart drug design[3].

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> **Theranostics is like the guardian of personalised medicine, where these drugs are built to both find and fight diseases. In oncology, these special drugs act like super-sensitive molecular probes, shining a light in the anatomical site where cancer is hiding and at the same time acting as targeted radiotherapy. Theranostics show us a perfect blend of scientific innovation, practical knowledge, and patient-centric approach. This is changing the way we deliver medicines, guiding us toward precise treatments that focus on effectiveness, safety, and the well-being of each person.**

2 - Source: www.nejm.org/doi/full/10.1056/NEJMp1500523
3 - Source: www.nature.com/articles/s41591-022-01717-2

Precision oncology in the works: radiotheranostics

In the last few years, we have witnessed a renaissance of nuclear medicine applied to cancer diagnostics and treatments, namely radiotheranostics or simply **theranostics** – cell-killing radiation strategies that combine molecular targeting and optimised radiation dosimetry. These molecules represent a remarkable fusion of science and innovation, shaping up a transformative era in medicine. The evolution of radiolabelling techniques has allowed for the precise development of radiopharmaceuticals, paving the way for targeted drug delivery. Theranostics is where diagnostics and treatment meet, pushing nuclear medicine into a time of incredible precision and patient-focused care. These drugs play a double role as theranostic agents, smoothly shifting from diagnosing to treating. By smartly picking certain radioactive elements and teaming them up with selective molecule expressed in cancer tissues, these agents catch cancer early, figure out their anatomical location, and monitor treatments resulting in one of the best approaches in precision oncology. Lutathera and Pluvicto are among the few successful approved theranostics for neuroendocrine and prostate cancers, respectively.

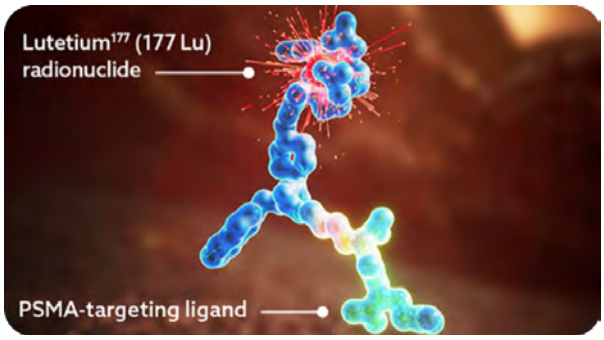
> **The fusion of AI with radiopharmaceuticals not only enhances diagnostic and therapeutic outcomes but also accelerates research and drug development, transforming the discovery of novel theranostics with optimised radiotracers and therapeutic agents.**

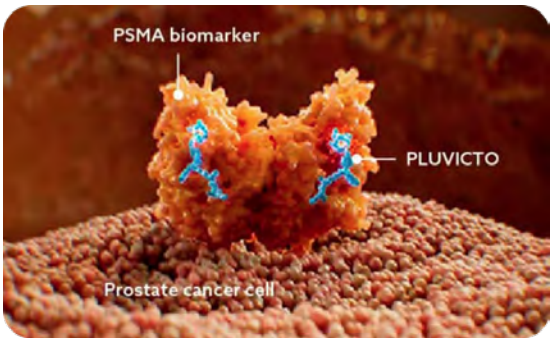
AI shaping the next generation of radiopharmaceuticals

Like in many other fields of oncology, AI plays a crucial role in theranostics' clinical development from imaging analysis to therapy delivery, incorporating patient-specific factors, radiotracer biodistribution profiles, and dosimetry calculations.

This combination boosts the accuracy of radiopharmaceutical imaging with AI algorithms efficiently navigating through vast datasets to reveal subtle patterns and anomalies that might escape human detection. Theranostics may function in multiple ways: improving cancer detection, precise disease staging, and non-invasive evaluation of treatment effectiveness. Many imaging and therapeutic radionuclides are conducted with the same molecule exchanging the imaging and therapeutic radionuclides. As a result, this type of AI-guided radiopharmaceuticals light the way to optimal diagnosis, treatment, and, ultimately, improved patient well-being.

Theranostics, a breakthrough in prostate cancer treatment





Source: Candriam, Novartis

> **Our team of Biotechnology experts monitors closely the evolving oncology landscape and seeks to invest in companies developing the most promising precision oncology strategies with a high probability of success.**

Focusing on the most promising companies and drugs

Cancer is a difficult and complex enemy with multiple subtypes or histologies. It is also constantly changing in response to therapy. As cancer patients live longer, the cancer journey may entail chronic treatments with the need for sequential treatments using multiple therapeutics alone and in combinations to further improve 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**. For lung cancer, over 30 new targeted drugs were launched during the past decade. As a result, over the past five years the usage of non-selective chemotherapy has been the fastest-shrinking treatment option, replaced by novel targeted therapies and combinations of immunotherapies leading to increased survival[4].

In the past two years, 27 new targeted therapies were approved in precision oncology[5], opening up new options for genetically and histologically defined subtypes of tumors. **For 2025, we expect this trend to continue with the approvals of new targeted therapies** for hard to treat cancers like colorectal, prostate, urothelial and pancreatic cancers, indications that are currently void of precision oncology options. We expect that novel targeted therapies will allow to tackle originally classified undruggable tumors, like RAS-addicted tumors.

4 - Source: New Report: Lung Cancer Survival Rate Improves, But Gaps in Biomarker Testing and Lack of Screening | American Lung Association
5 - Source: Citeline Pharma R&A Annual Review 2023 and 2024

Investing in Healthcare Stocks: a dynamic defensive segment in the currently challenging macroeconomic environment

Healthcare stocks tend to historically be a defensive play compared to the broad market, less vulnerable to economic cycles and inflationary pressures. They are backed by powerful and lasting forces:

- Healthcare companies mostly have bolstered balance sheets with growing revenues, less impacted by higher financing costs. Besides, consumption of medicines is not economically sensitive as diseases need to be treated regardless of economic conditions.
- The need of treating life-threatening diseases keeps evolving, fostering the discovering, funding, and development of new drugs and treatments. These come with high pricing, high margins and significant clinical markets.

As the fight against cancer is a long-term struggle, the stream of opportunities is far from drying up.