

# Innovations in Oncology

## The Future of Cancer Treatment

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ACF Equity Research

Anda Onu, Renas Sidahmed, Christopher Nicholson

Something is changing in oncology. We believe it is beginning a migration out of the surgery theatre - it feels like strands of a revolution are coming together.

By way of example, IceCure (NasdaqCM : ICCM) Medical's ProSense® System treatment test in Early-Stage Breast Cancer confirmed 100% tumour reduction in February 2024. The aim of the treatment is to destroy tumours by freezing them (cryotherapy) instead of removing them surgically. Cryotherapy offers a minimally invasive alternative to surgical removal, with benefits such as a reduced recovery, lower risk of complications, preservation of healthy tissue and suitability for high-risk patients where surgery is risky.

Cryotherapy is often performed as an outpatient procedure involving less post-operative pain and lowering the cost of the procedure. It can be repeated as needed making it a viable option for treating tumours with minimal psychological and physical impact on patients.

- According to World Health Organization (WHO) cancer, as a leading cause of death, is killing ~10m people per year globally. New cancer cases are expected at ~35m in 2050E, up 77% from 20m cases in 2022E (WHO, 2024).
- There is an ongoing battle to improve cancer treatment and diagnoses using various approaches such as AI, DNA sequencing, precision oncology, etc. (News Medical, 2023).
- The UK's National Health Service (NHS) is using a fast-acting cancer treatment injection (Atezolizumab), which is administered in seven minutes versus the typical hour-long infusion (Reuters, 2023).
- We [ACF Equity Research] are working with a client developing a pill based cancer therapy, one of the advantages of which is that, if successful, it looks as if it will not require any theatre time and only very minimal hospital time to administer and manage.

## Cancer Treatment Modalities (current approaches)

Cancer treatment includes various modalities tailored to combat the disease. Treatments may be used alone or combined, depending on the type of cancer, stage, location, and the patient's health and preferences. Key treatments include:

- **Surgery:** Surgical removal of cancerous tissue still remains a core treatment with ~45m surgical procedures required p.a., especially for localized tumours (Global Surgery Unit, 2018). We infer that a migration is occurring away from surgery, initially via a reduction in surgery time and invasiveness and ultimately away from the hospital and into the pharmacy.
- **Chemotherapy:** A staple treatment for many cancers that involves using drugs, of which there are 100+ existing types (e.g. alkylating agents, anti-tumour antibiotics, topoisomerase inhibitors) to kill or slow the growth of cancer cells (VeryWell Health, 2024).
- **Radiation Therapy:** High-energy particles/waves are used to destroy or damage cancer cells. ~50% to 60% of all cancer patients receive radiation during their care, alongside surgery, or as a standalone treatment (AdvaMed, 2024).
- **Immunotherapy:** A treatment that boosts the body's natural defences to fight cancer using monoclonal antibodies, checkpoint inhibitors (allow the immune system to switch back on, particularly T-Cell reactivation), CAR-T cell therapy, cytokines and vaccines. Immunotherapy has gained prominence, particularly for cancers like melanoma and lung cancer (Cancer Research UK, 2024).
- **CAR T-cell Therapy:** An immunotherapy that modifies patients' white blood cells (T-cells) to recognise and attack advanced leukaemias and lymphomas. Globally, ~34k patients received commercial CAR-T cell immunotherapies in early 2024E. CAR T therapies have huge potential and are just in the early stages of developing a market footprint. By way of illustration, in 2022A there were ~20m new cancer cases worldwide (International Society for Cell & Gene Therapy, 2024 & WHO), CAR-T therapies have been applied to the equivalent of just 0.17% of the 2022A new cancer cases estimate.
- **Stem Cell Therapies:** [Bone Marrow Stem Cells \(BMSCs\)](#) are used to repair tissues damaged by cancer or its treatment, particularly in blood-related cancers.
- **Precision Medicine (Genomic Testing):** Customises treatment using AI based on an individual's genetic makeup to maximise survival and quality of life. While genomic testing is becoming more common, its global adoption varies.
- **Cryotherapy:** Extreme cold is used to freeze and kill cancer cells. It is mainly employed for localised tumours, skin cancers, and prostate cancer. See IceCure above.
- **Pharmaceuticals:** Traditional chemotherapy and newer targeted drugs focus on eliminating cancer cells. As of 2023A there were 193 oncology novel active substances (NASs - "new molecular or biologic entities or combinations where at least one element is new") launched globally (IQVA, 2024).

### Costs of Oncology Treatments

Oncology treatments costs vary widely, influenced by the technology's novelty, treatment length, and geographic location. Among the most expensive treatments are:

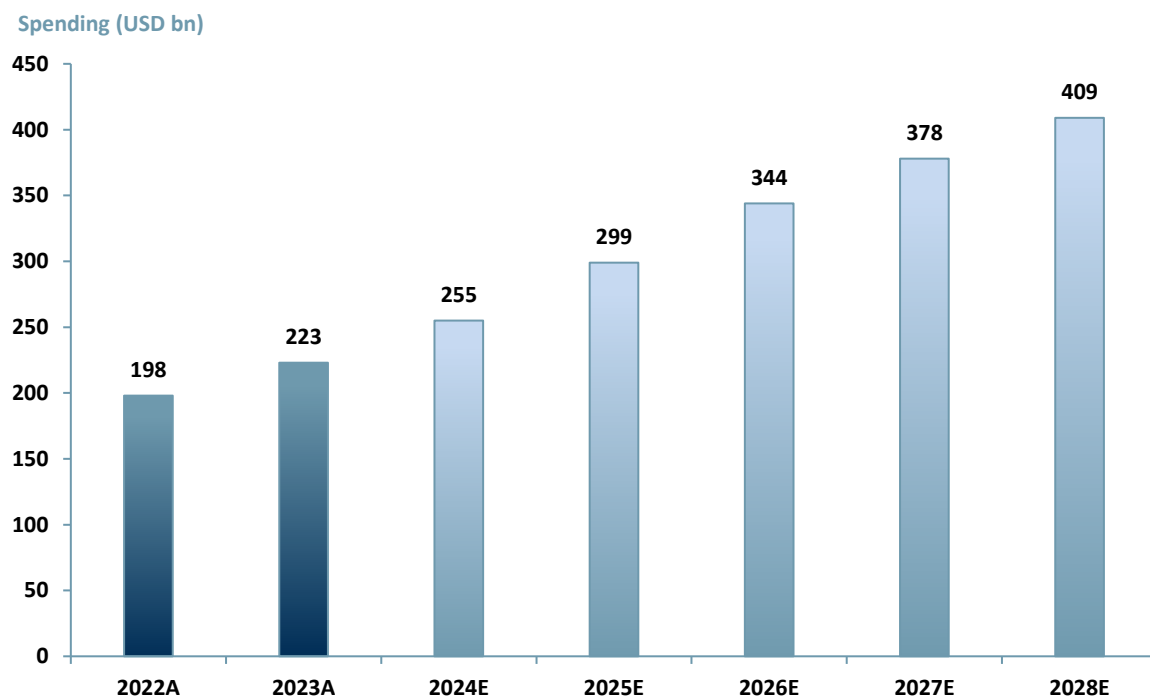
- **Stem Cell Therapies** - average cost ranges from ~US\$ 150k to 170k for autologous stem cell therapies. Autologous stem cells are cultured and modified using a patient's own stem cells, usually bone marrow derived, as the stem cell source. Currently, autologous stem cell therapies minimise rejection risk and more effectively persuade the body's own immune and other systems to repair itself.
- **CAR T-cell Therapy** - average cost ranges from US\$30,000 to US\$1m (DVCStem, 2020, WebMD, 2023, Nature, 2024).

Global oncology spending is projected to reach US\$409bn by 2028E, up from US\$223bn in 2023A at a 5yr CAGR of 11.5-14.5% from 2024-2028 (IQVIA, 2024). This growth is in part driven by US spending, which has increased to \$99bn in 2023A up from \$65bn in 2019A - the US makes up ~45% of global oncology spending.

Pharmerging markets (countries that have smaller pharmaceuticals markets than hyper developed economies, but that therefore have potential for increased uptake (growth), e.g. India, China, Russia, Brazil, Mexico, South Africa, Turkey, and Indonesia) are also contributing to the drivers for oncology spending growth (IQVIA, 2024). In part, these so-called pharmerging markets are leveraging off-patent drugs (off-patent therapies are characterised by brand loss of exclusivity (LOE).

Once a globally branded drug or therapy comes off-patent, their market shares are rapidly eroded by far less expensive generics or biosimilars in these markets. What is more, the market for such off-patent drugs is increasing because falls in market prices encourage greater usage. Compare the decline in solar power component prices and the effect on that market, which is becoming more valuable through greater up-take, year on year.

Exhibit 1 - Global oncology treatment spending forecast 2022A - 2028E



Sources: ACF Equity Research Graphics and Estimates; IQVIA 2024.

### Companies Involved in Cancer Treatment

Some of the most notable recent cancer treatment breakthroughs are from companies including Roche (Swiss: ROG), Novartis AG (NYSE: NVS), Bristol-Myers Squibb Company (NYSE: BMY), Gilead Sciences (Nasdaq: GILD) and IceCure Medical Ltd. (NASDAQ: ICCM), we [ACF Equity Research] expect our pill based oncology client to join this club in due course.

Companies leading in these technologies are well-positioned for growth, particularly as global healthcare systems increasingly prioritise innovative and cost-effective treatment modalities.

- **Roche (Swiss: ROG)** offers pharmaceutical products for anaemia, blood and solid tumours, amongst other therapeutic areas. ROG is known for ‘Avastin’, which is used in treating various cancers including colorectal and lung cancer.
- **Novartis AG (NYSE: NVS)** focuses on therapeutic areas such as cardiovascular, renal and metabolic, immunology, neuroscience, and oncology. NVS is a pioneer in CAR T-cell therapy with ‘Kymriah’, treating acute lymphoblastic leukaemia (Novartis, 2024).
- **Bristol-Myers Squibb (NYSE: BMY)** offers products for oncology as well as for immunology and neuroscience diseases. Its ‘Opdivo’ product for lung cancer and melanoma is just one of the multiple oncology treatments.
- **Gilead Sciences (Nasdaq: GILD)** is a biopharmaceutical company that develops medicines in unmet medical needs internationally. Through its subsidiary Kite Pharma, it produces ‘Yescarta’ for certain types of non-Hodgkin lymphoma.
- **IceCure Medical Ltd. (NASDAQ: ICCM)** specialises in minimally invasive cryoablation therapies. It's primary technology ‘ProSense’ platform destroys tumours by freezing them with liquid nitrogen. This method is particularly used for treating breast, kidney, and lung cancers.

Exhibit 2 - Peer group of companies focused on oncology treatments

TTM Metrics / Company Name	Market	Tkr	MCAP \$(m)	EV \$(m)	EBITDA \$(m)	FCF \$(m)	RoA	RoE
	XFRA	RHO6	220,709	248,927	22,017	12,044	20.22%	41.19%
Bristol-Myers Squibb Comp	XNYS	NVS	208,777	226,592	18,828	10,148	33.88%	34.58%
	XNYS	BMY	81,297	129,376	17,436	12,509	-13.93%	-23.01%
	BVMF	GILD34	15,107	35,583	10,826	7,900	1.97%	2.32%
	XNAS	ICCM	35	25	-15	-13	-91.90%	-102.91%
Average							N/M	N/M
Median							1.97%	2.3%

Sources: ACF Equity Research Graphics; Statista, Refinitiv.

Understanding the spectrum of oncology treatments and what we see as relatively rapid recent progress and innovations in some of the modalities, leads us to infer that a round of significant progress in cancer care is approaching. For investors and healthcare professionals alike, keeping abreast of these advancements is crucial in navigating the future of oncology treatment and so where returns might best be achieved (as modified by investor risk profiles).

## Strategic Monitoring for Stakeholders

To maximise the benefits from these advancements in oncology treatment, stakeholders including investors should focus on several key areas:

- **Regulatory Developments:** Changes in regulatory policies can significantly impact the approval, adoption, and commercialization of new oncology treatments. Regulatory bodies like the FDA (Food and Drug Administration) and EMA (European Medicines Agency) determine the market readiness of new therapies. Monitoring regulatory updates, approval timelines, and any changes in the guidelines, offer key perspectives on factors (capex, time, remaining IP protection period, weighted average cost of capital and so NPV). that affect the timing of the market entry of innovative treatments.
- **Market Adoption Rates:** The speed and extent to which new treatments are adopted by healthcare providers and patients are crucial indicators for total available likely or possible investment returns. Factors influencing adoption rates include clinical efficacy, cost-effectiveness, ease of integration into existing treatment protocols, and overall patient outcomes.
- **Ongoing Clinical Trial Results:** Clinical trials are the backbone of medical advancements in oncology. They provide critical data on the safety, efficacy, and potential side effects of new treatments. Regularly reviewing results from ongoing trials, and Phase I-III studies, can help investors assess the viability and future prospects of emerging therapies, they tend to be under appreciated by markets when the phase trials go well.

On the other hand missing the primary and secondary outcomes in a phase trial, though heavily penalised by markets that fear company collapse, can lead to markets failing to grasp post-hoc analysis implications - there can be significant overlooked/uncrystallised value in the details of the peer reviewed trial results and other papers, providing extraordinary returns opportunities for the persistent and informed.

*Note that high quality investment/equity research coverage that covers the technical aspects (as well as valuation) in an accessible way is an essential ingredient that almost all investors should have access to before embarking on investments in this particular sector.*

**Authors:** Anda Onu, Renas Sidahmed, Christopher Nicholson - Anda is part of ACF's Sales & Strategy team; Renas is Head of ESG and a Staff Analyst at ACF Equity Research; Christopher is Head of Research at ACF. [See their profiles here](#)