MARKET OVERVIEW OF GLOBAL ONCOLOGY MARKET

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By

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Under the Supervision and Guidance of

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HEALTHARK

Organization Certificate

Date: 19/06/2024

This is to certify that **Kavya Bahuguna** in partial fulfillment of the requirements for the award of the degree of MBA (Hospital and Health Management) from the IIHMR University, Jaipur has successfully completed her internship at Healthark Insights during 18th March 2024 to 18thJune 2024.

Sincerely,
Amol Pandya
HR Manager
Healthark Insights

DECLARATION BY THE STUDENT

I hereby declare that this dissertation titled **Market Overview of Global Oncology Market** is the bonafide record of my original research work. I declare that it has not been submitted to any other university or institution for the award of any degree or diploma. Information derived from the published or unpublished work of others has been duly acknowledged in the text.

Dr. Kavya Bathuguna

19th March 2024

CERTIFICATE

This is to certify that dissertation titled "***Market Overview of Global Oncology Market***" is a record of the research work undertaken by Kavya Bahuguna in partial fulfillment of the requirements for the awardof the degree of MBA (Hospital and Health Management) from the IIHMR University, Jaipur under my guidance and supervision and his/her approach to the research study has been sincere, scientific, and analytical.

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ABSTRACT

Cancer is a growing global health crisis with a projected rise in new cases to 29 million by 2040. Lung cancer is the most common, followed by breast, colorectal, prostate, and stomach cancers. Breakthroughs in science, mergers and acquisitions, and a focus on targeted therapies are transforming oncology. However, disparities in access to these advancements pose a significant challenge.

The field of oncology continues to be at the forefront of biomedical innovation, with significant strides made in understanding cancer biology, developing novel therapies, and improving patient outcomes. As the global burden of cancer persists, the oncology landscape undergoes continuous evolution, driven by advancements in research, regulatory approvals, and market dynamics. This dissertation presents a comprehensive analysis of the oncology landscape, encompassing various dimensions such as global sales trends, top-performing drugs, regulatory approvals, mergers and acquisitions, recent drug approvals, ongoing clinical trials, breakthrough therapies, and future trends in cancer therapy.

By examining these dimensions, the study contributes to a deeper understanding of the evolving oncology landscape and its implications for patients, healthcare providers, researchers, and stakeholders.

The rationale behind taking up this research on the Market overview of global oncology market is that the field of oncology is experiencing an unparalleled period of change due to incredible scientific progress, evolving regulatory frameworks, and increased merger and acquisition activity. A thorough analysis is essential to comprehend market trends, recognize major stakeholders, and forecast future developments.

The study was carried out with the following objectives:

- To assess the global market and trends for the top oncology drugs
- To study the main factors driving advancements in oncology drugs
- To explore the latest advancements in cancer treatment and diagnosis

The research methodology used for this was an observational study using scientific databases like PubMed, and ClinicalTrials.gov. Regulatory Agency Websites: US Food and Drug Administration (FDA), European Medicines Agency (EMA). Pharmaceutical company's website: product pipelines,

recent mergers and acquisitions, and clinical trial results. News Articles and Industry Publications, journals, corporate annual reports, white paper.

This research highlights that the oncology market is witnessing a surge in targeted therapies, leading to increased healthcare spending but offering new hope for patients. Emphasis is shifting towards personalized medicine with drugs tailored to individual cancer profiles. While the overall number of oncology trials remains stable, there's a fascinating trend – a surge in the development of drugs targeting specific antigens like HER2 and Trop-2. Phase II trials for lung, breast, and blood cancers make up a large portion of ongoing research.

While PD-1/PD-L1 inhibitors remain dominant, new targets beyond these established immune checkpoint molecules are being explored, including LAG-3. The future of oncology is bright with the development of next-generation biotherapeutics, including mRNA vaccines. This personalized approach holds immense promise for improved cancer treatment outcomes.

Overall, the oncology landscape is undergoing a dynamic transformation marked by groundbreaking advancements, targeted therapies, and the pursuit of personalized medicine. However, ensuring equitable access to these innovations alongside continued research into novel treatment modalities remains crucial in the fight against cancer.

ACKNOWLEDGMENT

The completion of this dissertation would not have been possible without the invaluable participation and assistance of many individuals, whose names may not all be listed here. Their contributions are deeply appreciated and sincerely acknowledged.

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Additionally, I owe a profound debt of gratitude to my parents and family members for their unwavering support and encouragement. Their inspiration and assistance, whether direct or indirect, were instrumental in the successful completion of this study. Their belief in my capabilities has been a constant source of motivation throughout this journey.

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Dr. Kavya Bahuguna

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1. INTRODUCTION

Cancer has become a global health crisis, with its burden increasing at an alarming rate. In 2022 alone, over 20 million new cases were diagnosed, and this number is projected to rise to a staggering 29 million by 2040 due to a continuously growing and aging population. This exponential growth in cancer incidence is driving significant changes within the oncology market.

Lung cancer is the most common cancer worldwide, with 2.5 million new cases, representing 12.4% of all new cases. Female breast cancer was the second most common, with 2.3 million cases (11.6%), followed by colorectal cancer with 1.9 million cases (9.6%), prostate cancer with 1.5 million cases (7.3%), and stomach cancer with 970,000 cases (4.9%).

The pace of development in oncology has quickened, leading to a surge in new drug approvals compared to previous years. This intense competition among biopharmaceutical companies is also fostering mergers and acquisitions, alongside the rise of biosimilars as well as future trends (e.g. use of ctDNA).

The oncology landscape is undergoing a transformative era driven by groundbreaking scientific advancements, a shifting regulatory environment, and a surge in mergers and acquisitions. A comprehensive analysis is crucial to not only grasp current market trends and identify key products but also to anticipate future developments in this dynamic field.

Cancer research is experiencing a surge of new, targeted therapies, significantly influencing healthcare expenditure. These treatments present new possibilities for patients previously ineligible for traditional options. Nevertheless, disparate accessibility to these advancements poses a substantial obstacle. Anticipate the continuation of established trends and novel developments in cancer treatment within the next five years.

1.1 OVERVIEW

TRENDS IN CANCER INCIDENCE AND MORTALITY

The incidence of cancer is projected to increase significantly by 2050, especially in lower-income countries, with an expected rise of over 12 million new cases each year. This escalating disease burden highlights the critical necessity for developing new treatments that can improve both survival rates and quality of life for affected individuals. Disparities in 5-year cancer survival rates among countries, even those with similar levels of GDP, suggesting that distinct healthcare strategies may result in better outcomes for certain types of cancer. The varying severity and progression of cancer, along with differences in healthcare systems, indicate that tailored approaches may be more effective for specific

types of cancer, such as early detection or initiatives dedicated to improving survivorship and quality of life. Sharing best practices and benchmarking across countries could facilitate addressing differences and optimizing care for cancers that display significant variations in survivorship.

ONCOLOGY RESEARCH AND DEVELOPMENT ACTIVITIES

In 2023, there was a noticeable decline in the initiation of oncology trials, but they remained 11% higher than in 2019, with a particular focus on treating solid tumors. The involvement of emerging biopharma companies in these trials was striking, accounting for 60% of the total, which marked a significant increase from 33% a decade earlier. Notably, companies based in China have been taking on a more prominent role in clinical research, representing 35% of trial initiations in 2023, compared to just 5% a decade ago. Excitingly, novel treatment modalities such as cell and gene therapies, antibody-drug conjugates (ADCs), and multi-specific antibodies hold great promise for cancer treatment and are gaining traction in clinical research. Globally, fifteen ADCs have been approved, and the number of trials investigating this targeted chemotherapeutics has surged by 26% in 2023, signaling a growing interest from pharmaceutical companies. Furthermore, there are currently ten bispecific antibodies available for oncology treatment, and many more are in late-stage development, particularly for solid tumors. The exploration of radioligand therapies for various tumors, particularly prostate and neuroendocrine tumors, is ongoing, with the potential for these novel modalities to be used as standalone treatments or in combination with other innovative therapies. It's important to note that the development of these novel treatments is being expedited through collaborative efforts between regulatory agencies and the industry, leveraging artificial intelligence to advance the discovery of new therapies.

ONCOLOGY CLINICAL DEVELOPMENT PRODUCTIVITY

In 2023, the success rate for oncology composite increased to 10%, marking significant improvements across all phases, particularly in rare oncology and solid tumor research. Despite the persistent complexity of oncology trials, the level of complexity reduced by 8% since 2019, in contrast to a 2% increase in complexity for other disease areas. It's important to note that trial complexity varies across indications within oncology and the type of drug being tested. The number of subjects enrolled in clinical trials in 2023 decreased by 11% from its peak in 2021. Notably, Western European countries are the most frequently included in trials, but China and North American country inclusion has seen significant increases in recent years. Although there has been a reduction in trial durations, the overall duration of oncology programs has only been shortened by five months, mainly due to an increase in the white space, which refers to the time between trial completion and the starting of the next phase.

NOVEL ACTIVE SUBSTANCES IN ONCOLOGY

In 2023, a total of 25 new and innovative oncology drugs were introduced worldwide, bringing the cumulative number of such substances launched since 2014 to 192. However, the availability of these medicines varies significantly across different regions. The introduction of new medicines in Europe has slowed down, leading to delays in access to innovative treatments compared to the U.S. It's noteworthy that 27% of oncology drugs approved in the U.S. over the past decade are still not available in Europe. In 2023, the U.S. welcomed 18 new cancer medicines, most of which are tailored for rare cancers, genetically engineered, and often approved based on a single clinical trial. Meanwhile, the European Medicines Agency (EMA) approved 8 novel substances for blood cancers and 5 for solid tumors in 2023, which represents a decrease compared to the previous year. It's important to mention that many of these groundbreaking medicines receive approval for additional indications after their initial launch, expanding access to effective treatments. Interestingly, emerging biopharma companies took the lead in launching 61% of the new oncology drugs in 2023, introducing 45% of the total.

CANCER PATIENT ACCESS AND USE OF SCIENTIFIC ADVANCES

The global provision of cancer treatment regimens has been steadily increasing by an average of 9% per year since 2019. This growth is fueled by rising cancer rates and improved access to care. However, the introduction of new cancer therapies varies widely across different countries. Discrepancies exist in biomarker testing rates, the adoption of innovative treatments, and the availability of infrastructure to deliver advanced therapies. The use of checkpoint inhibitors has experienced a significant surge, but there are substantial differences in usage among countries on a per capita basis. These therapies are now being administered earlier in the course of cancer treatment and for a wider range of tumors. Recent advancements in the treatment of women's cancers, prostate cancer, and late-stage multiple myeloma have emerged with the introduction of novel modalities such as antibody-drug conjugates, radiopharmaceuticals, bispecific antibodies, and CAR T-cell therapies, which have shown promising outcomes for patients.

SPENDING ON ONCOLOGY MEDICINES

The global expenditure on cancer medication saw a significant increase to $223 billion in 2023, and experts anticipate that it will climb to $409 billion by 2028. This growth can be attributed to the emergence of new products and the sustained presence of patented brands, despite the loss of exclusivity for certain treatments. The widespread adoption of biosimilars in major markets has led to substantial cost reductions. Notably, spending on six major tumor categories surged by double digits, driven by the

introduction of breakthrough medicines and improved patient accessibility. PD-1/PD-L1 inhibitors, widely utilized in solid tumor treatments, accounted for $52 billion in spending in 2023, and this figure is expected to escalate to over $90 billion by 2028. The potential future of next-generation biotherapeutics in oncology is presenting clinical and commercial uncertainties, yet annual expenditure could potentially surge from $4 billion to $23 billion by 2028.

2. REVIEW OF LITERATURE

The global health threat posed by cancer continues to grow, with over 20 million new cases diagnosed in 2022. Experts anticipate this number to climb to a staggering 29 million by 2040 due to factors such as population growth and aging. This surge is significantly impacting the field of oncology. Lung cancer ranks as the most common type, followed by breast, colorectal, prostate, and stomach cancers.

However, the pace of cancer research has accelerated, resulting in more new drug approvals than ever before. This intensified competition is also driving consolidation in the biopharmaceutical industry, as well as the development of biosimilars and potentially groundbreaking new approaches like ctDNA analysis.

The oncology market is undergoing significant transformation due to scientific breakthroughs, evolving regulations, and increased consolidation. A comprehensive analysis is critical to comprehend current trends, identify key products, and anticipate future developments in this rapidly changing field.

New, targeted cancer therapies are emerging, offering hope for many patients who may not have benefited from traditional treatments. However, unequal access to these advancements remains a major challenge.

Table 2.1

Title of study	Author	Learning
Global Oncology Trends 2024: Outlook to 2028	IQVIA Institute for Human Data Science	Cancer cases are expected to rise significantly, especially in developing countries. New, targeted therapies are being developed, with a focus on cell and gene therapies and antibody-drug conjugates. These novel treatments are showing promise but require specialized care and can lead to access disparities. Spending on cancer medicine is projected to nearly double by 2028.
Pharma R&D Annual Review 2024	Ian Lloyd, Jonathan Stephens, Sydney Enokawa, Tollan Bell, Abdirazak Mohamed, JT Toebbe, and Arbesa Bela	The report forecasts future trends in the pharmaceutical industry, similar to how weather forecasts predict sunshine or rain. The industry is booming due to factors like COVID-19 but faces challenges from climate change. The report will analyze areas of high and low growth, providing insights for future planning.
An analysis of FDA-approved drugs for oncology	Michael S. Kinch	Cancer drug approvals have soared since 1990. While biotech companies lead the way in early research, pharmaceutical giants end up with most approved drugs. Interestingly, nearly

		half of these new drugs target a specific protein type, kinases, with a focus on tyrosine kinases.
An Arm and a Leg: The Rising Cost of Cancer Drugs and Impact on Access	Natasha B. Leighl, Sharon Nirmalakumar, Doreen A. Ezeife, Bishal Gyawali	The soaring prices of cancer drugs have led to a global access crisis, with low- and middle-income countries being particularly affected. This financial burden disproportionately impacts younger patients, recent immigrants, and those without private insurance. Calls are growing for pricing based on regional costs and for oncologists to discuss treatment affordability with patients.

3. RESEARCH METHODOLOGY

3.1 Type of study: Desk review based on secondary data from published articles/reports

3.2 Research Question: What are the top-selling oncology drugs globally, and what factors contribute to their sales trends and driving forces?

3.3 Research Objectives:

- To assess the global market and trends for the top oncology drugs
- To study the main factors driving advancements in oncology drugs
- To explore the latest advancements in cancer treatment and diagnosis

3.4 Methodology

3.4.1 Inclusion criteria

- Studies focusing on oncology drugs, reports on market access, and analysis
- Studies published between 2015 and 2024

- Publications in English language

3.4.2 Exclusion criteria

- Articles that did not focus on market access and analysis for oncology
- Articles published in a language other than English
- Articles published before 2015

4. RESULTS

4.1 ONCOLOGY REVIEW

Despite reaching a massive USD 169.4 billion, the global oncology drug market has seen a slight slowdown recently, with Immunology, Neurology, and Diabetes now vying for the top spot. This market encompasses a diverse range of cancer treatments, from targeted therapies and chemotherapy to immunotherapies and hormone therapy. Breast cancer remains the most common type treated, followed by blood, lung, bladder, kidney, thyroid, and other cancers.

The highest oncology drug sales are attributed to Keytruda gaining revenue of USD 20.9 B and is expected to be the best-selling drug next year due to its expansion strategy and broadening indication Revlimid (10.1), Opdivo (9.3), Imbruvica (8.4) and Darzalex (8.0) are also among the top-selling drugs

Companies are actively pursuing mergers and acquisitions to strengthen their presence in oncology, either by expanding their flagship products or diversifying their pipeline with new drugs. This ongoing consolidation has positioned F. Hoffmann-La Roche Ltd (including Genentech), Bristol Myers Squibb, Pfizer, and Johnson & Johnson as the dominant players in the global oncology market.

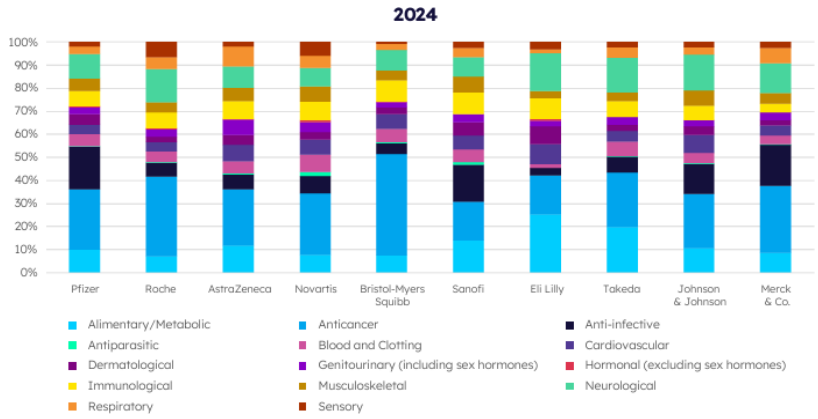

Fig.1 Disease focus areas of the Top 10 pharma companies. Source: Pharmaprojects®, January 2024

TOP ONCOLOGY DRUGS BY SALES

1) **KEYTRUDA | Merck ($20.9 B)**

   Keytruda first approved by the FDA in 2014, is a type of immunotherapy used to treat melanoma, NSCLC, classical HL, HNSCC, urothelial carcinoma, MSI-H or dMMR and GEJ adenocarcinoma. It is the first FDA-approved tissue-based broad CDx that is validated for all solid tumors.

   Keytruda sales growth in the US benefited from increased uptake across recent launches in earlier-stage indications such as breast cancer, melanoma and renal cell carcinoma

2) **REVLIMID | Bristol Myers Squibb ($10.1 B)**

   Lenalidomide, marketed as Revlimid by Celgene Corporation, was first FDA-approved for multiple myeloma (MM) treatment in 2005. It faces competition in the US from generic versions by Teva and Dr. Reddy's Laboratories.

   The FDA-approved generic versions of Revlimid in the US from Dr. Reddy's Laboratories Ltd and Teva USA led to a 32% decrease in revenues because of reduced demand caused by generic erosion.

3) **OPDIVO | Bristol Myers Squibb | ($9.31 B)**

Opdivo received its initial FDA approval in 2014 for treating patients with unresectable or metastatic melanoma. This prescription medication is utilized for treating HNSCC, urothelial carcinoma, MSI-H or dMMR metastatic colorectal cancer, RCC, melanoma, NSCLC, and classical HL. Its notable advantage over its competitor Keytruda is that it does not necessitate biomarker testing.

4) **IMBRUVICA | Johnson & Johnson | Abbvie | ($8.4 B)**

   Imbruvica received its first FDA approval on November 13, 2013 for treating MCL in patients who have undergone at least one previous therapy. Following that, the drug has been approved for CLL, SLL, WM, marginal zone lymphoma, and cGVHD.

   The market size of Imbruvica is projected to reach USD 66.29 billion by 2030, with an expected growth rate of 6.9% from 2022 to 2030.

5) **DARZALEX | Johnson & Johnson | ($8.0 B)**

Daratumumab, sold under the brand name Darzalex, is utilized for the treatment of adults with multiple myeloma and light chain AL. Clinical trials are being carried out by Janssen to assess the effectiveness and safety of Darzalex in combination with other medications for addressing different types of cancer.

The increase in Darzalex sales is due to the acquisition of market share in every region and the successful adoption of FASPRO. Darzalex FASPRO, a subcutaneous formulation released in 2019, enables patients to receive doses within minutes, a significant improvement compared to the previous intravenous administration which took hours.

6) **TAGRISSO | AstraZeneca | ($5.4 B)**

The oral medication is prescribed for adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) who have specific mutations in the EGFR gene, including T790M mutation-positive NSCLC. Authorized for use in over 90 countries, it received its first FDA approval for NSCLC in 2020.

Tagrisso became the company's highest-earning drug due to the increased demand for NSCLC treatment worldwide.

7) **IBRANCE | Pfizer | ($5.1 B)**

Ibrance, produced by Pfizer, received approval from the EMA in 2016. Originally granted accelerated approval by the FDA in 2015, the medication is indicated for the treatment of locally advanced or metastatic breast cancer.

Sales decreased as a result of scheduled price cuts that were recently implemented in established international markets. Additionally, there was a rise in the number of patients obtaining Ibrance through the US Patient Assistance Program, although this was partly balanced out by increased sales in various regions.

8) XTANDI | Pfizer | Astellas | ($5.0 B)

Xtandi is approved for treating metastatic and castration-resistant prostate cancer in men, when used alongside androgen deprivation therapy. Global sales of the drug have shown a growth rate (CAGR) of 17% from 2019 to 2022.

The rise in sales is a result of consistent demand growth in all areas and an increase in the number of uses for prostate cancer.

9) PERJETA | Roche | ($4.5 B)

Perjeta is approved for use alongside trastuzumab and docetaxel for the neoadjuvant therapy of individuals with HER2-positive, locally advanced metastatic breast cancer. The exclusive marketing rights for Perjeta ended in the US in June 2024 and in Europe in March 2023.

The rise in Perjeta sales is primarily attributed to sustained high demand in the international market, particularly in China, where there is increasing demand for early and metastatic breast care treatments.

10) TECENTRIQ | Roche | ($4.1 B)

Tecentriq, a form of cancer immunotherapy called a PD-L1 inhibitor, assists the immune system in identifying and combating cancerous cells. Given the green light by the FDA, it is recommended for initial treatment of adult patients with metastatic NSCLC, HCC, Urothelial Carcinoma, SCLC, and unresectable or metastatic melanoma.

Fig.2 Top-performing drug by sales.
Source: Cancer compass: Advances, approvals & regulatory updates. Healthark Insights. 2023

4.2 MERGERS AND ACQUISITION

Biotechnology companies are feeling the pressure to innovate and expand their oncology portfolios due to the looming issue of patent expiration. As a result, more companies are acquiring to catch up on research and development for specialty drugs, particularly those targeting rare cancer diseases. The fierce competition among big pharmaceutical companies and biotech firms for oncology drugs, along with the high valuations of late-stage companies, is prompting companies to engage in earlier-stage deals. Engaging in early-stage ventures allows pharmaceutical companies to influence the trajectory of a program and provide funding for more clinical programs, thus increasing the likelihood of success.

The major deals are as follows:

The acquisition will significantly boost Pfizer's position in the Oncology sector by integrating Seagen's expertise in Antibody Drug Conjugates (ADCs) and their advanced-stage development projects. Seagen anticipates generating around USD 2.2 billion in revenue in 2023, which reflects a 12% year-over-year growth. This revenue is expected to be derived from Seagen's four existing medicines, as well as from royalties and various collaboration and licensing agreements. The proposed merger will effectively double Pfizer's early-stage oncology clinical pipeline, broadening its portfolio, which currently focuses on breast cancer, genitourinary cancer, hematology, and precision medicine.

The recent deal significantly supports BMS's long-term growth strategy by providing a portfolio of highly precise oncology treatments. Turning Point's key asset, repotrectinib, stands out as a cutting-edge tyrosine kinase inhibitor that targets ROS1 and NTRK mutations. This drug has garnered three fast-track designations from the FDA and is anticipated to achieve sales of USD 1.1 billion as a first-line treatment and USD 0.5 billion as a second-line treatment specifically for lung cancer. Additionally, Turning Point is also developing four other experimental drugs in the clinical stage, with three of them classified as targeted therapeutic treatments.

GSK is showing strong support for Sierra Oncology's groundbreaking JAK inhibitor, momelotinib, following an unsuccessful pivotal Phase III trial for Blenrep. As a result, momelotinib will stand as GSK's only blood cancer product on the market for 2023. In its pursuit of FDA approval, GSK has also commenced discussions with experts to explore potential additional applications for momelotinib.

Sobi's recent acquisition is a significant milestone in the company's strategic plan to establish a prominent presence in the rare hematology sector. The acquisition is set to enhance and complement Sobi's existing portfolio, particularly in the areas of blood-related cancers and rare diseases. CTI, a biopharmaceutical company with a strong focus on rare diseases, aligns seamlessly with Sobi's leading hematology franchise. Notably, CTI brings VONJO, a groundbreaking oral kinase inhibitor, to Sobi's portfolio.

Sumitovant Biopharma will have the capacity to expedite the execution of its management strategies through the revenue streams generated by Myovant's two approved products, Orgovyx and Myfembree. This acquisition will empower Sumitovant to broaden the influence of Myfembree and Orgovyx, and further propel its ongoing clinical program opportunities. Additionally, Myovant Sciences will contribute its clinical pipeline for the treatment of prostate cancer, urinary diseases, pediatric illnesses, and respiratory ailments, thereby expanding Sumitovant's reach in addressing various medical conditions.

The acquisition of Aveo by LG Chem's Life Sciences Division will allow LG Chem to establish a strong commercial presence in the US market and expand its portfolio with a diverse range of Oncology Therapies. This strategic move will enable LG Chem to introduce Aveo's lead product, Folvida, which has already been granted FDA approval for treating adult patients with relapsed or refractory advanced RCC after previous systemic therapies. In addition to Folvida, Aveo has three other promising cancer candidates in its pipeline. One of these candidates is ficlatuzumab, currently undergoing phase I testing for head and neck cancer, with expectations to obtain FDA approval by 2030.

The recent acquisition represents a significant expansion of the company's technology base and product offerings. The addition of ModeX's diverse portfolio enhances our pipeline with a range of multi-specific and multi-functional antibodies tailored for various types of cancers and other therapeutic areas. Notably, ModeX's product lineup includes innovative cancer immunotherapies that incorporate four specificities into a single protein. These advanced therapies are designed to enhance targeted immune killing while leveraging "stealth" technology to improve tumor-specific killing and reduce potential side effects.

Gilead's acquisition will significantly expand Kite Pharma's pipeline, particularly in the development and application of its approved cell therapies, Yescarta and Tecartus. Additionally, as part of the deal, Kite will gain access to future innovations through a sponsored research and license agreement with the University of Pennsylvania. The acquisition also includes the integration of seven programs from Tmunity, with at least four of them already listed in studies posted on the federal clinical trial registry.

4.3 TRENDS IN CANCER INCIDENT AND MORTALITY

The prevalence of cancer is expected to rise notably by 2050, particularly in countries with lower incomes. In the next 25 years, there will be over 12 million new cases of cancer annually. The forecasted disease burden emphasizes the critical need for innovative treatment options to enhance both survival rates and quality of life.

Disparities among countries in the five-year survival rates for cancer indicate significant variations, even in countries with similar levels of GDP. Differences in five-year survival rates between countries suggest that implementing specific care system strategies for different types of cancer could lead to better outcomes. While there have been considerable enhancements in survival rates for the deadliest tumors in the U.S., the survival rates for many of these tumors remain low.

Tumors differ in their seriousness and rate of advancement. Due to these differences, as well as health system variations among countries, implementing different healthcare strategies may be more effective in improving outcomes for certain types of cancer. For tumors with low survival rates and relatively consistent outcomes across countries, early detection is crucial for improving survival. This will involve various methods such as screenings, more frequent interactions with healthcare providers, and providing advanced biomarker and imaging tests to a larger number of patients. In the case of tumors with higher survival rates and varying outcomes across countries, focusing on the aspects of care that improve survivorship and/or quality of life may lead to more consistently better results.

In situations where tumors show significant variation across countries, countries may benefit from comparing their results with those of other nations. This comparison could lead to real-time adjustments of protocols or care strategies.

Cancer diagnosis rates are projected to rise by 61% by 2050, highlighting the crucial importance of ensuring uniformity in providing care, fair access to healthcare, and ongoing enhancements in the range of available treatments.

The occurrence of cancer is expected to rise substantially by 2050, particularly in countries with lower incomes.

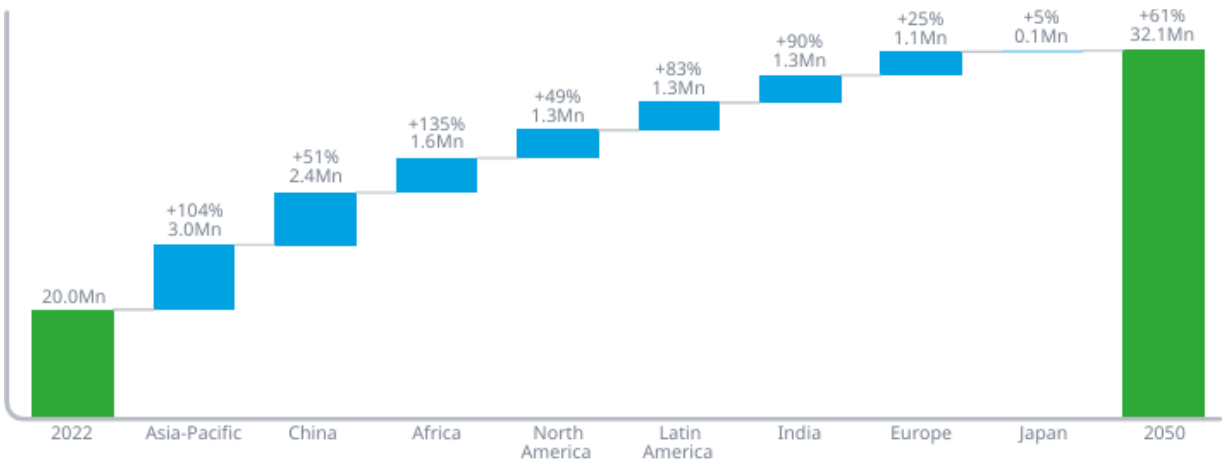

Fig. 3 All cancer incidence(millions) in 2022 and projected growth to 2050
Source: IARC Global Cancer Observatory

In the next 25 years, there is an expected rise of over 12 million new cancer cases annually. The projected increase is focused mainly in less prosperous regions worldwide, primarily due to economic growth, longer life expectancies, and greater exposure to cancer risks later in life. These projections emphasize the pressing need for new treatment options to enhance survival rates and quality of life. More than half of the rise is anticipated in Asia, with China leading the way with an estimated 2.4 million additional cases annually by 2050, marking a 51% increase from 2022.

In the coming years, India is expected to experience a 90% increase, adding 1.3 million cancer patients annually. Meanwhile, Japan's cancer rates are expected to remain stable due to its aging and declining population. The collective group of other Asia-Pacific nations is projected to see a 104% rise in cancer cases by 2050. Africa's cancer diagnoses are anticipated to increase by 135%, resulting in 1.6 million more cases by 2050, while Latin America is expected to see an 83% increase. Finally, North America is expected to have 49% more cancer diagnoses, totaling 4 million by 2050.

4.4 RECENT DRUG APPROVALS

1) **ELACESTRANT**
Indication: Breast cancer

Indicated for treating advanced or metastatic breast cancer with disease progression following at least one line of endocrine therapy in postmenopausal women or adult men with estrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2)-negative, and ESR1-mutated breast cancer.

2) **PIRTOBRUTINIB**
Indication: Lymphoma

The medication is produced by Eli Lilly and Company and is used to treat adult patients with relapsed or refractory MCL after they have received at least two rounds of systemic therapy, including a BTK inhibitor, as approved by the FDA. Additionally, it has received conditional marketing authorization from the EMA for the identical indication.

3) **RETIFANLIMAB-DLWR**
Indication: Merkel Cell Carcinoma

MacroGenics, Inc.'s Zynyz received accelerated approval from the FDA on March 22, 2023. It is approved for treating metastatic or recurrent locally advanced MCC in adult patients.

4) **EPCORITAMAB**
Indication: Lymphoma

Produced by AbbVie and Genmab, this is the initial and singular bispecific antibody medication. It is prescribed for managing relapsed or refractory DLBCL in adult patients, not otherwise specified, including DLBCL stemming from slow-growing lymphoma, and high-grade B-cell lymphoma following two or more rounds of systemic treatment.

5) **FLOTUFOLASTAT F 18**
Indication: Prostate cancer

This is applicable for using PET to detect PSMA-positive lesions in males diagnosed with prostate cancer who are considered for initial definitive treatment or suspected of recurrence based on increased serum PSA level. Adding Posluma to the NCCN Clinical Practice Guidelines in Oncology could potentially raise the drug's utilization in clinical settings and broaden the market for Blue Earth

4.5 ONCOLOGY RESEARCH AND DEVELOPMENTACTIVITIES

The past decade has witnessed a significant shift in oncology research, with a growing emphasis on developing targeted drugs that leverage innovative mechanisms to combat cancer. This targeted approach aims to deliver more precise treatment options with potentially fewer side effects compared to traditional therapies. However, despite this shift, the overall number of oncology clinical trials has remained relatively stable as of 2023.

Within this stable number, a fascinating trend emerges a surge in development efforts for drugs targeting specific antigens. Notably, 28 products are currently in development to target HER2, a protein found on the surface of some cancer cells, while another 12 focus on Trop-2, another shared antigen present in various solid tumors. This intense focus on specific targets highlights the potential of personalized medicine, where treatments are tailored to a patient's unique cancer profile.

Looking deeper into the clinical trial landscape, Phase II trials, which aim to assess the effectiveness of a new treatment in a larger group of patients, currently constitute the largest segment at 49%. These trials often focus on lung cancer, followed closely by breast cancer. Interestingly, blood cancers, such as lymphoma and leukemia, also hold a significant presence in Phase II studies.

This focus on specific cancer types translates into real-world spending growth. Over the past five years, seven out of the top ten most prevalent tumors have experienced double-digit growth in medication spending. This surge can be attributed to breakthroughs in treatment options, offering hope for improved patient outcomes.

However, regulatory approval pathways may differ geographically. While the US Food and Drug Administration (FDA) has granted the highest number of breakthroughs for breast cancer, the European Medicines Agency (EMA) has prioritized designations for lung cancer, lymphoma, and myeloma. This highlights potential variations in the types of cancer receiving the most regulatory attention across different regions.

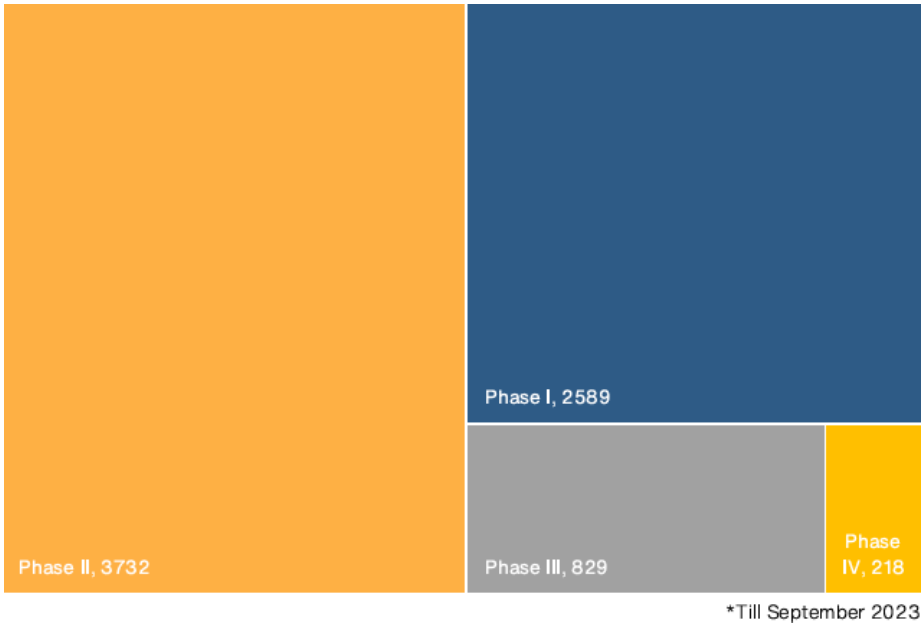

Fig.4 Oncology clinical trials

Source: Cancer compass: Advances, approvals & regulatory updates. Healthark Insights. 2023

One of the most striking observations from recent data is the dominance of Phase II trials. These trials, designed to assess the efficacy and safety of a promising treatment in a larger patient population after demonstrating some effectiveness in smaller, early-stage trials, constitute the largest portion of oncology trials. This highlights the importance of rigorously evaluating the effectiveness of potential therapies before moving them on to larger Phase III trials, which confirm their efficacy compared to existing standards of care.

While the overall number of oncology trials might appear stagnant, a closer look reveals some interesting trends. Notably, the focus on drug development for solid tumors, which are cancers arising from tissues (as opposed to blood cancers), remains strong. Trials targeting solid tumors comprised a significant 75% of all oncology trials initiated in the 2022-2023 period. This sustained focus suggests the ongoing need for more effective treatments for various solid tumor types, which remain a significant challenge in oncology.

However, the field does not neglect advancements in other areas. Hematological cancers, which affect the blood, bone marrow, and lymphatic system, are also witnessing a surge in research activity. The number of trials initiated for hematological cancer drugs has witnessed a noteworthy increase of 30% from 2017 to 2022, with over 550 new trials launched in this period. This significant rise points towards advancements in understanding the biology of blood cancers and the development of targeted therapies specifically for these types of malignancies.

In 2023, the number of new oncology trials decreased compared to previous years, but they were still 11% higher than in 2019. These trials were mainly targeted at researching rare cancers and solid tumors. Interestingly, a significant increase was seen in the involvement of emerging biopharma companies, accounting for 60% of the oncology trials in 2023, compared to only 33% a decade ago. Furthermore, there has been a substantial rise in oncology trials started by China-headquartered companies, increasing from 5% to 35% over the past decade. Notably, novel oncology mechanisms, such as cell and gene therapies, ADCs, and multi-specific antibodies, now make up a quarter of all trials. In addition, the introduction of PD-1/PD-L1 inhibitors in trials increased by 29% over the last five years. Of particular interest, oncology cell and gene therapy trials have been striving to advance CAR T-cell therapies, especially in the realm of hematological cancers. The year 2023 saw the commencement of over 250 trials examining CAR T-cell therapies in oncology, with a growing number focused on solid tumors.

Over the past five years, the global approval of fifteen antibody-drug conjugates (ADCs) has sparked a 22% annual increase in trial starts. In the field of oncology, ten bispecific antibodies are currently being marketed globally, with numerous others in various stages of development, particularly for the treatment of solid tumors. Ongoing trials are exploring the potential of radioligand therapies in addressing a wide range of tumors, with a focus on prostate and neuroendocrine tumors. The fast-paced evolution of multiple innovative treatment modalities holds great promise, both individually and in combination with one another. Regulators and industry stakeholders are pushing the boundaries of cancer drug development to accelerate access to solutions for patients. Furthermore, the growing evidence of artificial intelligence’s potential in advancing research candidates to clinical development is becoming increasingly apparent.

4.6 KEY DRIVING FACTORS

A) Emerging biopharma companies sponsored 60% of oncology trials in 2023, up from 33% a decade ago

The landscape of oncology clinical trials is undergoing a significant transformation, with a clear shift in leadership towards emerging biopharmaceutical companies. This trend, with its potential implications for both the pace of innovation and patient access to novel therapies, necessitates a closer examination.

Data from 2023 paints a compelling picture. Emerging biopharma companies, defined as those with annual sales below $500 million and research and development (R&D) expenditures capped at $200 million per year, have emerged as the driving force in oncology research. Remarkably, they now account for a commanding 60% of all clinical trials initiated in this field. This represents a near-doubling of their share compared to 2014 when they held a relatively modest 33% stake.

Conversely, large pharmaceutical companies, traditionally the dominant players due to their substantial resources, are witnessing a decline in their influence. Their share of trial initiations has shrunk considerably, dropping from a dominant 59% in 2014 to a mere 28% in 2023. This represents a significant 31-point decrease, suggesting a potential shift in priorities and capabilities within the established pharmaceutical industry.

While the overall number of oncologytrial starts has experienced a concerning 9% decline over the past two years, it is crucial to analyze the underlying dynamics. Notably, the growth in emerging biopharma trials has remained steady, demonstrating their unwavering commitment to oncology research despite potentially limited financial resources. This resilience stands in stark contrast to the 20% decline observed in trials initiated by large pharma companies, suggesting a potential retrenchment or change in focus within the larger industry.

However, the picture is not a binary one. While emerging biopharma companies have surged to the forefront, small and mid-sized pharmaceutical companies have also witnessed a decrease in oncology trial starts over the past two years. Despite this decline, it’s important to acknowledge that this segment still holds a larger collective share of trials compared to a decade ago. This suggests a potential consolidation within the non-large pharma space, with some companies exiting the oncology research

B) Novel oncology mechanisms, especially cell and gene therapies, ADCs, and multispecific antibodies have risen to 25% of trial starts

The past decade has witnessed a significant shift in the focus of oncology research and development (R&D). The spotlight has increasingly turned towards targeted drugs with innovative mechanisms, aiming to combat cancer with greater precision and potentially fewer side effects compared to traditional therapies. However, recent data reveals some interesting trends within this evolving landscape.

While the focus on targeted therapies remains strong, the landscape is not static. Clinical trials for hematological cancers, which affect blood, bone marrow, and the lymphatic system, experienced a notable decline of 17% in 2023. Conversely, development activity for solid tumor cancers, which form masses in tissues, has remained relatively stable after reaching a peak in 2021. This suggests a potential reprioritization within the research community.

One noteworthy trend is the declining growth trajectory of PD-1/PD-L1 checkpoint inhibitors. These drugs, which have revolutionized cancer treatment by harnessing the body's immune system to fight cancer cells, may be reaching saturation in the market. This decline suggests that researchers are exploring newer, more targeted molecules with the potential for improved efficacy.

Antibody-drug conjugates (ADCs) also continue to play a significant role in the fight against cancer. These engineered molecules combine antibodies with cytotoxic agents, aiming to deliver these cell-killing drugs directly to cancer cells. This targeted approach reduces the potentially harmful side effects associated with traditional chemotherapeutics. Notably, the focus of ADC development has primarily been on solid tumors, with a remarkable 80% growth observed in this area over the past two years. This underlines the potential of ADCs for more effective treatment of solid tumor malignancies.

Finally, the field of cell and gene therapy is experiencing significant growth. Clinical trials for these innovative approaches have risen steadily, now constituting a significant 25% of all trials for hematological cancers. This increasing focus reflects the potential of cell and gene therapy to revolutionize cancer treatment by modifying or replacing diseased cells or directly targeting the underlying genetic causes of cancer.

C) Starts of trials that include PD-1/PD-L1 inhibitors increased by 29% over the last 5 years

Pembrolizumab (Keytruda), the first PD-1/PD-L1 checkpoint inhibitor, marked a pivotal moment in cancer treatment when it received FDA approval for melanoma in 2014. Since then, the field has seen a dramatic expansion, with eight additional PD-1/PD-L1 inhibitors gaining regulatory approval for various hematological cancers and solid tumors (as detailed in Exhibits 33 and 34). However, recent data reveals a nuanced picture regarding the ongoing development and utilization of these groundbreaking drugs.

While the total number of global trials initiated for PD-1/PD-L1 inhibitors in 2023 did experience a slight decline of 7% compared to 2021, it remains significantly higher (by 53%) than the number initiated in 2018 (746 trials). This suggests continued interest in exploring the therapeutic potential of these drugs.

However, a closer look reveals a potential shift in focus. A striking trend observed in 2023 is that a majority (85%) of the over 3,000 ongoing Phase II and III clinical trials for PD-1/PD-L1 inhibitors are being conducted within a single country. This suggests that the development of these drugs might not necessarily prioritize accessibility for global markets. Further research is needed to understand the reasons behind this trend.

The current focus of PD-1/PD-L1 inhibitor trials in clinical settings also highlights a potential shift in strategy. Over 80% of these trials are currently in Phase II, which often involve a smaller patient population compared to Phase III trials. These Phase II trials primarily concentrate on solid tumors, with a particular emphasis on cancers like non-small cell lung cancer (NSCLC), esophageal cancer, liver cancer, and head and neck cancer. This focus suggests that researchers might be exploring new applications and refining existing uses of PD-1/PD-L1 inhibitors for specific tumor types within the realm of solid tumors.

D) Oncology cell and gene therapy trials are focused on CAR T, particularly in hematological cancers

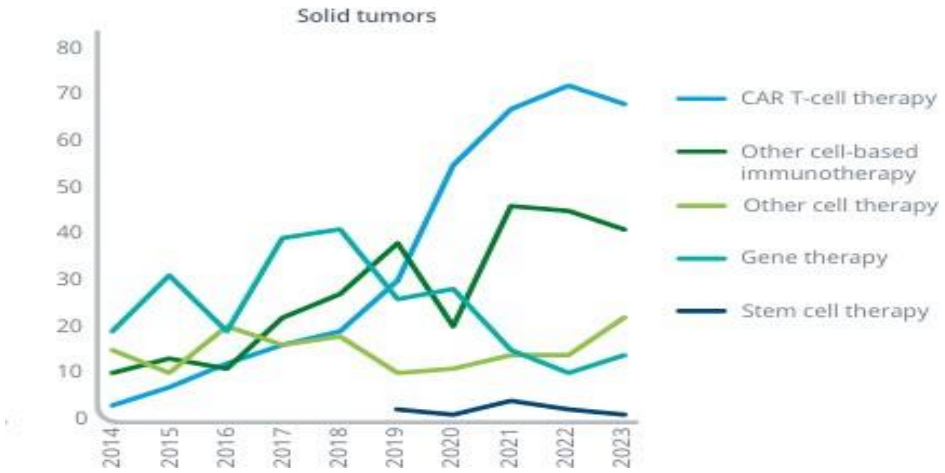

Fig.5 Oncology cell and gene therapy trials Phase I to Phase III by mechanism, 2014–2023.
Source: Citeline Trialtrove, Jan 2024; IQVIA Institute, Apr 2024.

The field of cell and gene therapy is experiencing a surge in activity, offering promising new avenues for cancer treatment. This trend is particularly evident when examining the data from 2023. Compared to a decade ago, the number of clinical trials investigating cell and gene therapy for both hematological cancers and solid tumors has witnessed a dramatic increase.

Chimeric Antigen Receptor (CAR) T-cell therapy has emerged as the dominant player within hematological cell and gene therapy trials. An impressive 80% of all hematological cancer trials in this area focus on CAR-T cell therapies, showcasing the immense interest and ongoing research dedicated to this innovative approach.

Another noteworthy trend is the rise of other cell-based immunotherapies for solid tumors. Clinical trials investigating T-cell receptors, tumor-infiltrating lymphocytes, and natural killer cell therapies have nearly quadrupled over the past decade. This surge indicates a growing interest in harnessing the body's immune system to combat these challenging malignancies. Gene therapy, particularly the use of gene editing tools like CRISPR, was previously a major focus within oncology cell and gene therapy trials. However, recent years have seen a slowdown in this area due to several safety concerns identified in clinical trials. Despite these setbacks, gene therapy still holds immense promise for future advancements in cancer treatment.

E) More than 250 trials testing CAR T-cell therapies in oncology started in 2023 with a growing number of solid tumors

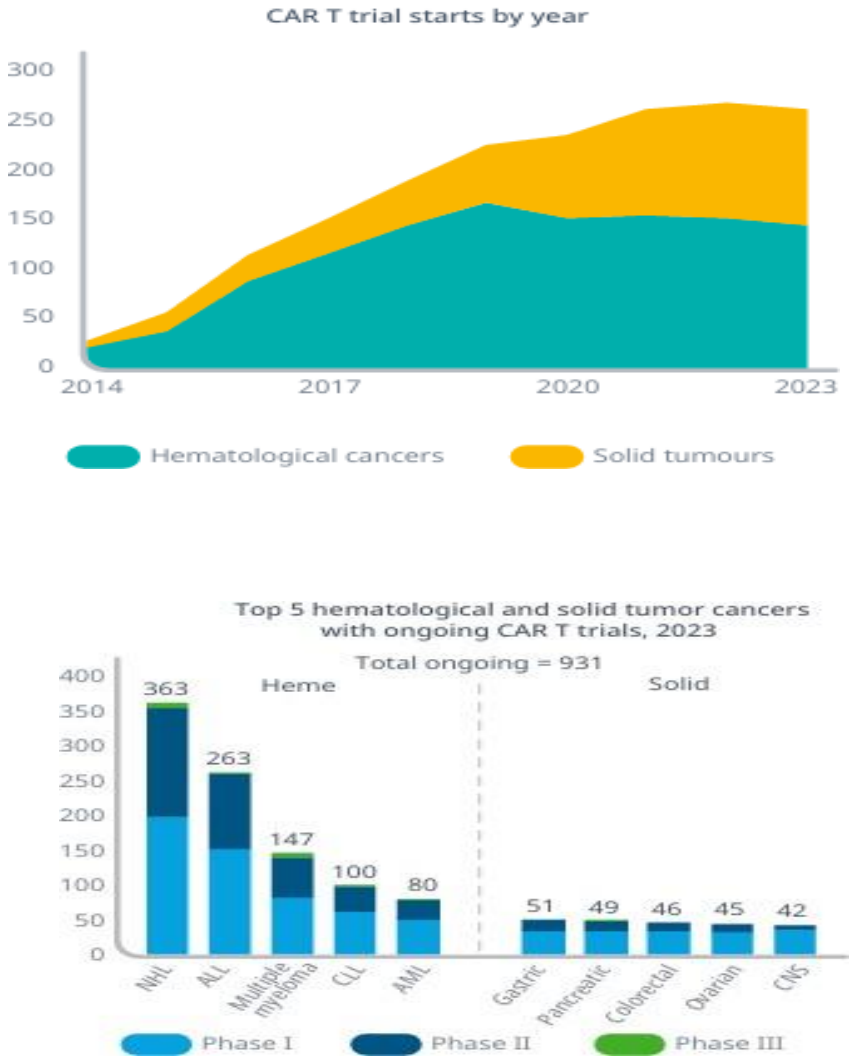

Fig.6 Oncology CAR T-cell therapy clinical trial starts and ongoing trials by top tumors
Source: Citeline Trialtrove, Jan 2024; IQVIA Institute, Apr 2024.

The past few years have witnessed a remarkable explosion of interest in CAR T-cell therapy, a revolutionary approach to treating cancer. Since the 2017 approval of tisagenlecleucel, the first CAR T-cell therapy for acute lymphoblastic leukemia (ALL), this field has seen significant progress. Eight additional CAR T therapies have been launched globally, targeting a wider range of relapsed or refractory hematological cancers (cancers of the blood, bone marrow, and lymphatic system).

While the momentum remains strong, with 264 new trials initiated in 2023 to study CAR T applications in oncology, a fascinating shift is taking place. While hematological cancer trial starts have remained consistent over the past five years, the number of trials focusing on solid tumors (cancers that form masses in tissues) has nearly doubled during the same period.

Historically, over 70% of CAR T trials have focused on hematological cancers. However, this trend is changing rapidly. In 2023, a significant 44% of all new CAR T trials initiated targeted solid tumors, a substantial increase from the 26% observed in 2019. This surge highlights the growing optimism and research efforts dedicated to adapting CAR T therapy for a broader range of cancers.

Currently, the majority (80%) of the ongoing 931 CAR T trials remain focused on blood cancers. Non-Hodgkin's lymphoma, a group of blood cancers, is a particular area of interest with 363 ongoing trials. However, the remaining 20% of ongoing trials for solid tumors represent a significant step forward.

F) Radioligand therapies are being tested across a range of tumors, primarily prostate and neuroendocrine

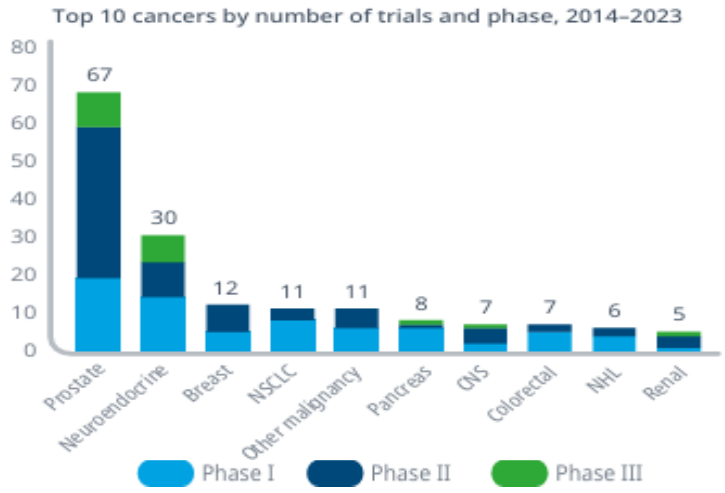

Fig.7 Top 10 cancers by number of trials and phase (2014-2023)
Source: Citeline Trialtrove, Jan 2024; IQVIA Institute, Apr 2024

Radioligand therapy (RLT) is emerging as a game-changer in cancer treatment. This innovative technique delivers radiation directly to cancer cells, minimizing damage to healthy tissues. The FDA has already approved two RLT drugs:

- **Lutathera (lutetium Lu 177 dotatate):** This drug is currently approved for neuroendocrine tumors, but researchers are exploring its potential for treating other cancers like breast cancer and Merkel cell carcinoma.
- **Pluvicto (lutetium Lu 177 vipivotide tetraxetan):** This therapy targets metastatic castration-resistant prostate cancer.

The past decade has seen a surge in RLT research, with 144 clinical trials initiated. Prostate cancer leads the pack with 67 trials, followed by neuroendocrine tumors (30 trials) and breast cancer (12 trials). Interestingly, the focus is primarily on solid tumors, with only 4% of RLT trials targeting non-Hodgkin's lymphoma (NHL), a type of blood cancer.

In essence, RLT offers a promising future for cancer treatment by precisely targeting malignant cells while minimizing side effects on healthy tissues. The ongoing research, particularly in prostate cancer,

neuroendocrine tumors, and breast cancer, holds immense potential for expanding treatment options for various cancers.

G) Regulators and industry sponsors are extending boundaries around cancer drug development to speed solutions for patients

The landscape of cancer treatment is undergoing a metamorphosis, marked by a pivotal shift towards the earlier deployment of groundbreaking therapies. This paradigm shift, characterized by the use of novel treatments as first-line therapy rather than traditional approaches, holds immense promise for improved patient outcomes. Regulatory bodies like the FDA are actively facilitating this evolution through initiatives such as Projects Frontrunner and Endpoint. These projects play a critical role by encouraging the adoption of novel endpoints that assess the effectiveness of these therapies when used earlier in the course of the disease. By providing robust data on the efficacy of early intervention, these initiatives pave the way for the seamless integration of these novel therapies into first-line treatment plans.

Another significant development is the remarkable evolution of biomarker screening, which is transforming our ability to identify and target specific mutations within cancer cells. We are witnessing a paradigm shift beyond traditional dedicated assays towards more sophisticated methods. The widespread adoption of next-generation sequencing (NGS) offers unparalleled precision in identifying genetic alterations, while the increasing accuracy of liquid biopsies (ctDNA) allows for minimally invasive assessment of tumor mutations through circulating tumor DNA in a patient's bloodstream. These advancements hold immense potential for personalized medicine approaches, enabling clinicians to tailor treatment regimens based on a patient's specific tumor profile. Additionally, researchers are actively developing less invasive testing methods to address the limitations of existing approaches.

As the number of treatment options and potential combinations continues to expand, a new challenge emerges: optimizing drug dosing for maximum therapeutic effect and extended response duration, while simultaneously minimizing the risk of subsequent resistance. This complex challenge is precisely what the FDA's Project Optimus aims to address. By focusing on optimizing treatment regimens through a data-driven approach, Project Optimus seeks to maximize the potential of these novel therapies and improve patient outcomes in the long run. By facilitating earlier intervention, utilizing sophisticated biomarker screening for personalized treatment plans, and optimizing treatment regimens, a multifaceted approach holds the key to unlocking the full potential of this new era in cancer treatment.

Themes in oncology R&D regulatory science

- Earlier lines of therapy

A new wave of highly effective cancer treatments is making a splash, replacing traditional approaches and becoming the go-to option (first-line therapy) for various cancers affecting both blood (hematological) and tissues (solid tumors). The US Food and Drug Administration (FDA) is playing a crucial role in this shift by spearheading Projects Endpoint and Frontrunner.

- Novel combinations to target drug resistance

As groundbreaking therapies become the standard first-line treatment (used earlier in the course of the disease), a concerning trend might emerge: a rise in patients resistant to the mechanisms and targets these therapies address. This is because the cancer cells have been exposed to these approaches earlier, potentially rendering them less effective.

- Evolving technology for biomarker sample collection

The field of biomarker testing is undergoing a rapid transformation. This includes:

- **Liquid biopsies (ctDNA):** These minimally invasive tests, which analyze circulating tumor DNA in the bloodstream, are gaining wider acceptance due to their increasing accuracy. This allows for a more convenient and patient-friendly way to assess cancer and potentially guide treatment decisions.
- **Expanding sample types:** Researchers are exploring the use of samples like feces, urine, and saliva for biomarker testing. This opens the door to even less invasive collection methods, potentially making testing more accessible and enabling more remote or virtual clinical trial designs. In simpler terms, these new sample types could eliminate the need for needles and allow for easier participation in clinical trials from the comfort of a patient's home.

- Minimum therapeutic dose in trials

Traditionally, cancer treatment trials have prioritized high drug effectiveness by using larger doses. However, this approach is believed to have downsides:

- **Increased toxicity:** Higher doses can lead to more severe side effects, potentially harming patients and limiting their ability to tolerate the treatment for a longer period.

- **Missed benefits:** Focusing solely on high-dose efficacy might have overlooked the potential for lower doses to be effective for some patients with fewer side effects. This could have meant missing opportunities for these patients to receive beneficial therapies for a longer duration.

To address these issues, the FDA's Project Optimus aims to change the approach. The project encourages drug manufacturers to establish the **optimal dose** for their therapies before moving on to larger registration trials. An optimal dose would strike a balance between effectiveness and tolerability, allowing patients to benefit from the treatment for a longer period with minimal side effects.

A) Evidence of the potential for AI has increased as research candidates advance into clinical development

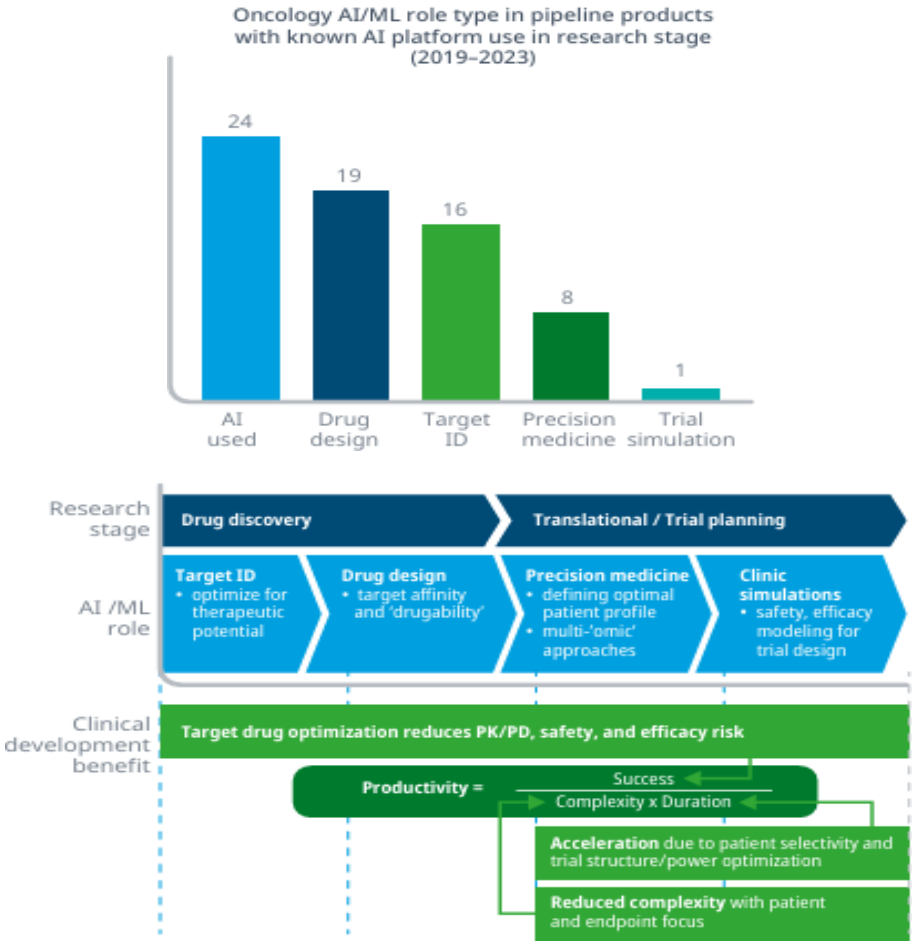

Fig.8 Impact of artificial intelligence (AI) on the industry clinical development pipeline

Source: Clinicaltrials.gov, Citeline Trialtrove, IQVIA Institute, Apr 2024

Artificial intelligence (AI) is rapidly transforming the landscape of drug discovery, particularly in oncology (cancer research). Here's a breakdown of the key points:

- **AI's Impact on Drug Discovery:** A significant portion (over 75%) of AI applications in oncology identified over the past five years focus on drug discovery and design. This suggests AI is being heavily utilized to develop and optimize new cancer treatments.
- **AI's Multifaceted Role:** AI isn't a single tool; it encompasses various techniques like large language models and analytical methods. In oncology research, these AI aspects often work together. For example, a single program might be used for target identification (finding the weak points in cancer cells) while simultaneously aiding in precision medicine approaches (tailoring treatments to specific patient needs).
- **Beyond Discovery:** This analysis excludes the growing field of AI-driven clinical process optimization. This involves activities like using AI to select suitable patients and trial sites, analyze pathology data, and interpret clinical trial endpoints.
- **The Future of AI in R&D:** As AI techniques become more sophisticated and widely adopted, they are expected to significantly improve the speed, efficiency, and cost-effectiveness ofcancer drug research and development.
- **AI's Broader Applications:** The benefits of AI extend beyond research. AI-powered tools are already assisting radiologists in interpreting medical images. As of October 2023, the FDA has approved nearly 700 AI/machine learning-based medical devices, with the vast majority (79%) used in radiology. These AI tools can potentially be integrated into clinical trials once they become established standards of care.

4.7 Cancer patient access and use of scientific advances

The global fight against cancer is seeing a significant boost, with the number of available treatment regimens increasing by an average of 9% annually since 2019. This surge is likely fueled by two factors: a rise in cancer cases worldwide and improved access to healthcare in many regions.

However, access to these new treatment options isn't always uniform. Disparities exist across countries regarding the use of molecular testing for different cancers and biomarkers. This variation can lead to discrepancies in the utilization of targeted medications, potentially impacting treatment effectiveness.

Encouragingly, the growing body of evidence supporting the efficacy of PD-1/PD-L1 checkpoint inhibitors has led to a shift in their application. Doctors are now incorporating them for pre-metastatic cancers (cancers that haven't spread yet), earlier lines of therapy, and across a wider range of tumor types.

The past three years have also seen a significant impact of immunotherapies, antibody-drug conjugates (ADCs), and PARP inhibitors on treatment patterns for cancers affecting women. These advancements offer promising new options for managing these often-challenging malignancies.

Finally, the introduction of novel radioligand therapies has led to an increase in the use of radiopharmaceuticals for advanced metastatic prostate cancer since 2021. This highlights the continuous development of innovative treatment strategies for various cancer types. While the number of centers providing CAR T-cell therapies is growing, these centers are spread out and do not offer all available products, which creates difficulties for patients who have to travel long distances and creates disparities for those who may not have the means to travel.

A) <u>The total number of cancer treatment regimens provided globally has increased by an average of 9% annually since 2019</u>

The global fight against cancer is witnessing a heartening trend: a steady rise in cancer treatment rates across developed markets. This growth can be attributed to two key factors:

- **Rising Cancer Incidence:** Unfortunately, the number of cancer cases continues to climb worldwide. This increased burden on healthcare systems necessitates a corresponding increase in treatment availability.
- **Improved Access to Care:** Encouragingly, access to quality healthcare is expanding in many regions. This allows for earlier diagnosis and facilitates the provision of potentially life-saving treatments.

While the situation in developed markets is improving, a crucial aspect of the global cancer battle lies in bridging the gap with lower-income countries. Here, efforts to widen access to care are yielding positive

results. Lower-income markets are experiencing an increase in the number of patients receiving treatment each year, driven by factors such as:

- **Expanding Access to Cancer Medications:** Initiatives to increase the availability of essential cancer medicines in these regions are playing a vital role. This allows for the implementation of effective treatment regimens for a broader patient population.
- **Longer Treatment Durations:** As treatment protocols evolve and become more sophisticated, treatment durations are often extended. This trend further contributes to the rising number of patients receiving ongoing cancer care.

The combined effect of these factors has resulted in a global average annual growth rate of 9% in cancer treatment regimens over the past five years. This represents a significant expansion in the fight against cancer.

However, despite the positive trends, a sobering disparity remains. Per capita, treatment rates in developed countries are still more than five times higher on average compared to lower-income and Pharmerging markets (emerging pharmaceutical markets). This stark difference highlights the need for continued efforts to ensure equitable access to cancer care on a global scale.

The promising news lies in the fact that Pharmerging and lower-income markets have witnessed the most significant growth in treatment rates over the past five years, with a compound annual growth rate (CAGR) of 12% and 10%, respectively. This indicates a positive trajectory towards bridging the gap in access to cancer care.

Looking ahead, the focus must remain on expanding access to essential cancer medicines, fostering robust healthcare infrastructure in developing regions, and promoting early diagnosis initiatives. By prioritizing these areas, and through continued advancements in cancer research and treatment, we can move closer to a future where everyone, regardless of location or socioeconomic background, has a fair chance of receiving effective treatment for this devastating disease.

B) Country-specific differences exist in molecular testing across different tumor types and biomarkers

Biomarker testing plays a critical role in personalized cancer care by identifying specific genetic alterations within a patient's tumor. These alterations can then guide treatment decisions, allowing for the selection of targeted therapies specifically designed to exploit these vulnerabilities. However, a concerning discrepancy is emerging between the rates of biomarker testing and patient access to the targeted therapies these tests might recommend. This disparity presents a significant challenge in ensuring equitable access to optimal cancer treatment across different geographic regions.

The National Comprehensive Cancer Network (NCCN) guidelines, a widely respected benchmark for oncology care in the United States, advocate for comprehensive biomarker testing in non-small cell lung cancer (NSCLC). These guidelines recommend testing all NSCLC patients for a panel of biomarkers, including EGFR mutations, ALK rearrangements, and PD-L1 status. Notably, data suggests that over 80% of patients in the U.S. undergo testing for most of these biomarkers. This reflects a positive adherence to established guidelines and potentially a more streamlined pathway to targeted therapies for patients with identified mutations.

In contrast, the European Society for Medical Oncology's (ESMO) NSCLC guidelines offer a somewhat different approach. While they recommend universal PD-L1 testing for all metastatic NSCLC patients, they suggest additional biomarker testing for a more select group of patients. This recommendation could explain the higher rate of PD-L1 testing observed in the EU4+UK region compared to testing for other biomarkers. This approach, while potentially cost-effective, raises concerns about potentially excluding some patients from potentially beneficial targeted therapies based on a less comprehensive testing strategy.

The situation with HER2 testing in breast cancer further highlights the complexities involved. Nearly all breast cancer patients undergo HER2 testing, as HER2 amplification is a well-established indicator of responsiveness to targeted therapies. However, a new challenge has emerged with the identification of HER2-low breast cancer. These tumors express lower levels of HER2, which may still respond to HER2-targeted therapies but were previously classified as HER2-negative. Unfortunately, accurately measuring these low HER2 expression levels remains a challenge with current assays. This highlights the need for continued development of more sensitive and reliable testing methods to ensure optimal patient selection

Furthermore, testing rates for biomarkers like tumor mutational burden (TMB) and microsatellite instability (MSI) are generally lower compared to other biomarkers. These biomarkers often suggest the applicability of tissue-agnostic therapies, which are effective against a specific genetic alteration regardless of the tumor's origin. This observation suggests that these potentially transformative therapies might be underutilized due to limited biomarker testing, potentially denying patients access to effective treatment options.

C) Although the number of CAR T-cell treatment centers is increasing, centers are dispersed and do not carry all products

CAR T-cell therapy, a revolutionary approach harnessing the power of a patient's immune system to fight cancer, offers immense promise for treating various hematologic malignancies. However, a crucial barrier currently hinders its potential: **unequal geographic distribution of treatment centers**. While a significant number of centers offer CAR T-cell therapy, their concentration around major population centers creates a significant logistical challenge for patients residing in more rural areas.

In the United States, for example, CAR T-cell treatment centers tend to be concentrated in large cities. This geographical disparity creates a burden for patients living in rural areas, who may face long and potentially arduous journeys to access these potentially life-saving therapies. The physical strain of travel, coupled with the complex logistics involved, can significantly impact treatment adherence and overall patient outcomes.

Even within regions with established CAR T-cell treatment centers, access to specific therapies can be restricted. Currently, in the U.S., only 45% of the 198 CAR T-cell treatment centers offer at least one product for each approved CAR T-cell therapy indication, including diffuse large B-cell lymphoma, follicular lymphoma, acute lymphoblastic leukemia, and multiple myeloma. However, a mere 22% of centers carry **all** currently available CAR T-cell therapies. This limited availability creates a complex situation where patients might need to travel significant distances to access the specific CAR T-cell therapy most appropriate for their individual case

To ensure equitable access to CAR T-cell therapy, a multifaceted approach is needed. Here are some key considerations:

- **Expanding treatment center reach:** Efforts to establish new CAR T-cell treatment centers in more geographically dispersed locations are crucial.
- **Collaboration and resource sharing:** Encouraging collaboration and resource sharing between existing treatment centers can optimize patient allocation based on therapy availability.
- **Financial assistance programs:** Implementing financial assistance programs can help alleviate the travel burden for patients from lower socioeconomic backgrounds.

By addressing these challenges and implementing a comprehensive strategy, we can move towards a future where CAR T-cell therapy becomes more readily available and geographically accessible to all patients in need, regardless of their location or socioeconomic background. This will ensure that this transformative treatment technology reaches its full potential in the fight against cancer.

D) Patient treatment rates for CAR T range from 25–70% of referred patients with reasons for non-treatment varying across countries

CAR T-cell therapy, a revolutionary approach harnessing the power of a patient's immune system to combat cancer, holds immense promise. However, the path to receiving this therapy is often fraught with complexities and barriers, ultimately preventing many eligible patients from accessing this potentially life-saving treatment.

The very first hurdle patients encounter lies in the eligibility assessment process. This involves determining if a patient meets the specific criteria for receiving CAR T-cell therapy. This assessment can take place at the center initially referring the patient, at the dedicated CAR T-cell treatment center, or through a hybrid approach involving both. Regardless of the chosen method, navigating this initial stage can be challenging, potentially delaying treatment initiation.

A concerning observation emerges when examining global treatment rates for CAR T-cell therapy. On average, across major markets, only 47% of patients referred for CAR T-cell therapy receive the treatment. This underscores the significant number of patients who fall through the cracks within the complex treatment pathway. Furthermore, this statistic hides a troubling disparity between countries. While some nations, like Italy, boast treatment rates as high as 70% for referred patients, others, such as Brazil, see a mere 25% of referrals translating into actual treatment. This stark difference highlights the need for a more standardized and equitable approach to CAR T-cell therapy delivery across the globe.

Reasons for Non-Treatment: A Complex Mix:

Understanding why patients don't receive CAR T-cell therapy is crucial to addressing these access disparities. While the reasons vary across countries, two primary factors emerge as the most common across all regions:

- **Disease Progression:** Unfortunately, by the time a patient is referred for CAR T-cell therapy, their cancer may have already progressed beyond the point where the treatment is effective.
- **Patient Fitness:** This therapy can be demanding, and patients with certain comorbidities or a weakened physical state may not be deemed suitable candidates.
- **Reimbursement Concerns:** Interestingly, reimbursement concerns appear to be a less significant barrier in most countries, with less than 30% of oncologists citing it as a factor.

Moving Towards a More Equitable Future:

To ensure that more patients have the opportunity to benefit from CAR T-cell therapy, a multi-pronged approach is necessary. Here are some key areas for focus:

- **Standardized eligibility criteria:** Establishing a more standardized approach to eligibility assessment can streamline the process and potentially identify suitable candidates earlier in their disease course.
- **Early referral:** Encouraging earlier referral for CAR T-cell therapy evaluation can help identify patients before disease progression becomes a limiting factor.
- **Improved patient fitness:** Developing strategies to improve patient fitness, potentially through pre-conditioning regimens, could widen the pool of eligible candidates.

- **Reimbursement solutions:** Addressing reimbursement challenges specific to certain countries, particularly the US and Brazil, is crucial to ensuring financial accessibility for patients.

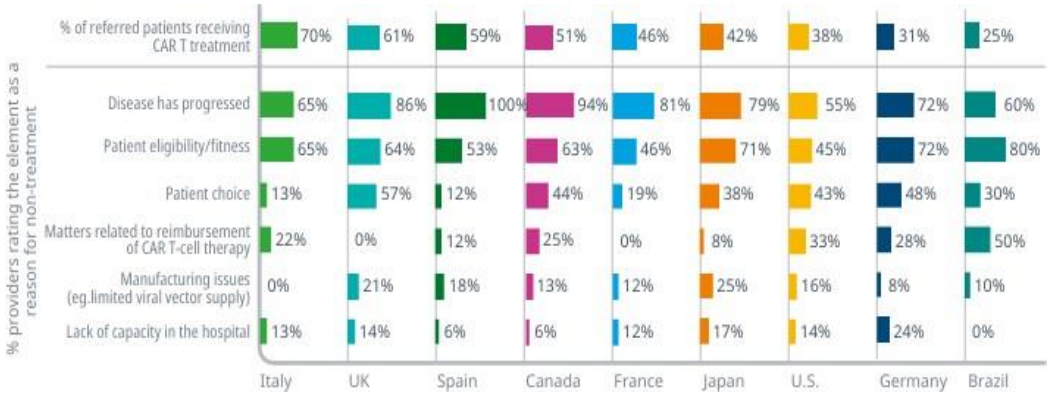

Fig. 9 Treatment rates and reasons reported for patients not receiving treatment, Q2 2023
Source: Strengthening Pathways for Cell and Gene Therapies: Current State And Future Scenarios, Mar 2024. Report by the IQVIA Institute for Human Data Science.

4.8 Global expenditure on oncology therapeutics

The global cost of cancer medications is on a steep upward trajectory. In 2023, spending reached a staggering $223 billion, and this figure is projected to nearly double by 2028, reaching an estimated $409 billion. This significant growth can be attributed to several key factors.

One major driver is the continued dominance of brand-name cancer drugs. These medications are protected by patents, allowing them to command high prices. Additionally, the recent launch of a wave of innovative cancer treatments over the past five years has further inflated overall costs.

Biosimilars, highly similar versions of existing biologics, are playing an increasingly important role in cost management. Their adoption rate in major markets has surpassed 50%, resulting in significant savings. In 2023 alone, biosimilars saved an estimated $7.1 billion, and the cumulative savings since 2017 total a substantial $19 billion.

One particular class of drugs, PD-1/PD-L1 inhibitors, exemplifies the high spending associated with innovative therapies. Used across most solid tumors, these drugs reached $52 billion in global spending in 2023 and are expected to exceed $90 billion by 2028.

Overall, the next five years are expected to see an 83% increase in global oncology medicine spending. This dramatic rise is primarily driven by innovation and the ongoing trend of expanding access to better cancer treatment options for patients worldwide. However, it is crucial to find a sustainable balance between fostering continued advancements and managing the associated costs to ensure these life-saving treatments remain accessible for all.

- **Cancer medicine spending rose to $223Bn globally in 2023 and is expected to reach $409Bn by 2028**

The global market for cancer medications is experiencing a significant upswing, with spending reaching $223 billion in 2023. However, a closer look reveals a geographically uneven distribution of these expenditures. Developed markets, encompassing the United States, the EU4+UK region (comprising the major European Union economies plus the United Kingdom), and Japan, account for a dominant 74% share of global cancer medicine spending. This concentration has remained relatively stable over the past five years.

Looking ahead, the spending trajectory in these established markets is expected to maintain a similar pace to the previous five years. Analysts project a compound annual growth rate (CAGR) of 11-14% through 2028 for both the US and EU4+UK regions. Japan, however, is anticipated to see a more moderate growth rate of 4-7% during this period.

The United States currently holds the top spot in terms of oncology spending, with expenditures reaching $99 billion in 2023. This represents a substantial increase from $65 billion in 2019 and translates to a commanding 45% share of global spending. Looking ahead, projections suggest a further rise to nearly $180 billion by 2028, solidifying the US position as the world's leading spender on cancer medications.

Finally, other developed countries outside the major established markets collectively accounted for $38 billion in cancer treatment spending in 2023. This category is projected to experience the highest growth rate of all regions, with a projected CAGR of 14.5-17.5% through 2028. This anticipated surge can be attributed to two key factors: a rising incidence of cancer in these populations and increased access to innovative new cancer medications.

The global landscape of cancer treatment spending paints a picture of progress, with increasing investment in novel therapies. However, the significant geographical disparities raise concerns about equitable access to these life-saving medications. Moving forward, a multi-pronged approach is needed. Continued research and development are crucial to ensure a steady stream of innovative cancer treatments.

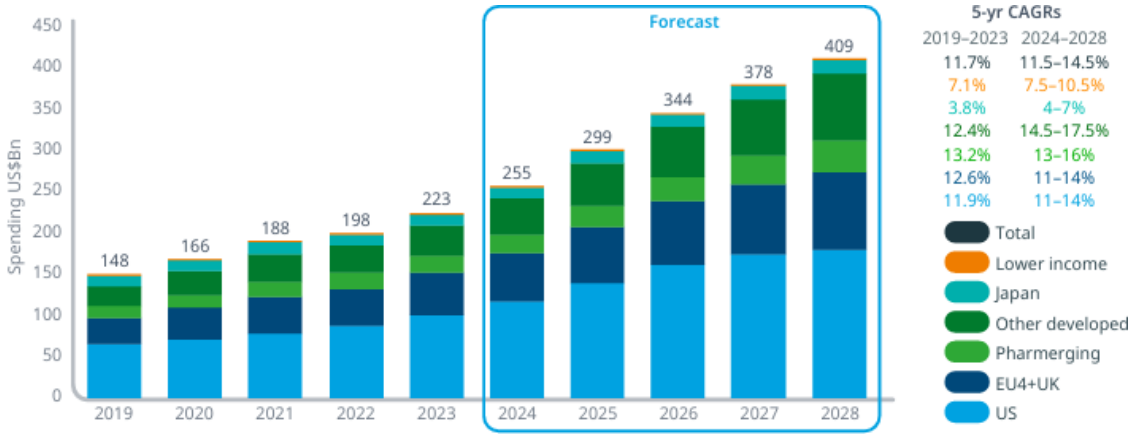

Fig.10 Oncology spending by region, US$Bn
Source: IQVIA MIDAS, Dec 2023; IQVIA Institute, Apr 2024.

- **<u>Oncology biosimilar uptake has been greater than 50% across major markets and biosimilars saved payers over $7Bn in 2023</u>**

Biosimilar medications, highly similar versions of existing biologic drugs, offer a significant opportunity to reduce treatment costs for both patients and healthcare systems. However, the rate of biosimilar adoption for cancer treatment varies considerably across different regions of the world.

Three key oncology molecules - bevacizumab, rituximab, and trastuzumab - have paved the way for biosimilar adoption in major markets. The first biosimilars for these drugs were launched in the EU4+UK region in 2017, followed by Japan in 2018 and the US in 2019.

The US healthcare system has witnessed the most rapid and widespread adoption of oncology biosimilars among these regions. On average, three years after launch, biosimilar uptake for these three key molecules reached an impressive 77% in the US. This highlights the potential cost savings biosimilars can offer, making them a particularly attractive option in the US healthcare landscape.

While the EU4+UK region initially saw quicker biosimilar adoption compared to the US, the pace of uptake has slowed down in recent years. Three years after launch, the average biosimilar uptake across the region reached 72%. However, significant variation exists between individual countries. For example, the UK has a lower average biosimilar uptake of 57%, while Germany boasts a considerably higher rate of 82%.

Japan presents a unique case. Due to its tightly controlled drug pricing and reimbursement systems, biosimilar uptake for oncology treatments has been lower compared to other major markets. After three years, biosimilar uptake stands at 52% in Japan.

Despite the variations in adoption rates, biosimilars have already delivered significant cost savings in major markets. Since 2017, biosimilars have generated an estimated $19 billion in savings, with over 61% of these savings concentrated in the US healthcare system. These cost reductions translate to lower treatment costs for patients and healthcare systems alike, ultimately enabling more patients to access these life-saving medications.

The future of biosimilars in oncology holds even greater promise for cost savings. Several key events are on the horizon in the next five years, with biosimilar versions of denosumab and immune-oncology checkpoint inhibitors expected to enter the market. The introduction of these biosimilars is projected to generate substantial additional savings, further improving the affordability and accessibility of cancer treatment across the globe.

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4.9 Future trends in oncology

The field of immuno-oncology, which harnesses the body's immune system to fight cancer, has witnessed a period of remarkable progress. However, the search for new therapeutic targets beyond the established PD-1 and CTLA-4 immune checkpoint molecules has taken some unexpected turns.

While PD-1/PD-L1 inhibitors remain a mainstay of oncology treatment, their clinical trial development has seen a recent shift. In 2022, the number of new global trials investigating these agents dropped by 11% compared to 2021. However, this decline should be viewed in context. The number of trials initiated in 2022 still represents a significant 54% increase over those initiated in 2017. This suggests a potential optimization phase, where researchers may be focusing on refining existing PD-1/PD-L1 therapies and exploring their efficacy in combination with other treatment options.

Antibody-drug conjugates (ADCs) are emerging as a promising class of cancer therapeutics. These targeted therapies combine monoclonal antibodies, which specifically recognize cancer cells, with potent cytotoxic drugs. Recent research suggests significant efficacy of ADCs across a broad range of targets, including Trop-2 and CEACAM5. This opens exciting possibilities for tailoring treatment to specific cancer types and potentially achieving improved outcomes.

The LAG-3 molecule has emerged as another potential target in immune checkpoint modulation. Early clinical trials investigating LAG-3 inhibitors, particularly in melanoma cases, have shown promising results. This paves the way for further exploration of LAG-3 blockade as a potential therapeutic strategy and potentially expands the options available for immunotherapy treatment.

The future of oncology holds immense promise with the ongoing development of next-generation biotherapeutics. The biotherapeutic pipeline is experiencing significant growth, with a noteworthy trend being the rise of mRNA vaccine research. In 2023, mRNA vaccines accounted for a substantial 8% of the biotherapeutic pipeline. This surge in interest highlights the potential of utilizing mRNA technology to create personalized and effective cancer vaccines.

A) Biotherapeutics

- **mRNA Revolution in Oncology**

The astounding success of mRNA vaccines in combating COVID-19 has ignited a surge in research and development for their application in cancer treatment. This exciting new frontier in oncology has witnessed a more than twofold increase in mRNA vaccine development since 2019, with a particular focus on targeting solid tumors.

One prominent example is the partnership between Merck and Moderna. Leveraging the well-established immune-boosting capabilities of mRNA technology, this collaboration aims to develop vaccines that specifically target cancer cells. The potential benefits are clear: by harnessing the body's own immune system, mRNA vaccines offer the promise of a more personalized and potentially more effective approach to cancer therapy.

Beyond standalone applications, mRNA vaccines are also being investigated in conjunction with existing cancer treatments. Numerous clinical trials are exploring the combined potential of mRNA vaccines and immuno-oncology agents, such as PD-1 checkpoint inhibitors. This multifaceted approach utilizes the ability of mRNA vaccines to stimulate the immune system, while checkpoint inhibitors further enhance the immune response by removing a key "brake" on the body's natural anti-tumor activity.

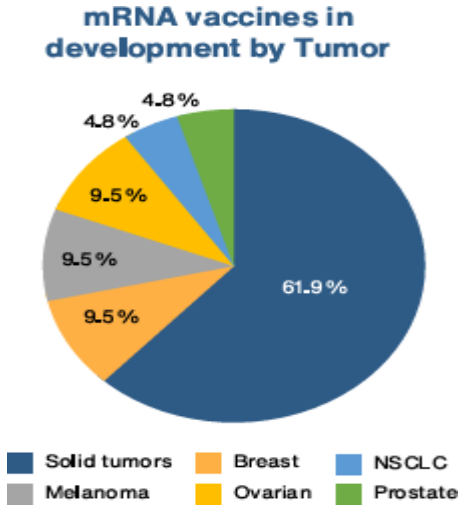

Fig.11 mRNA vaccines development by tumor

Source: Cancer compass: Advances, approvals & regulatory updates. Healthark Insights. 2023

- **Immunotherapy Evolves: Trials Explore Alternatives to PD-1/PD-L1**

The landscape of immuno-oncology (IO) clinical trials is undergoing a fascinating transformation. While 2022 marked the first year since 2018 that saw a decrease (2.86%) in the overall number of new IO trials compared to the previous year, this decline should be viewed in the context of a broader trend. This decrease can be attributed primarily to a 6.4% decline in the initiation of Phase IV trials, which often involve established treatment strategies.

Furthermore, the use of PD-1/PD-L1 inhibitors, while still a mainstay in IO therapy, is showing signs of saturation. The number of trials investigating these agents dropped by 10.3% in 2022. Conversely, other promising targets like CTLA-4, LAG-3, and CD3 T cell engagers are experiencing a surge in interest. These targets saw increases of 17.9%, 36.8%, and 13.3%, respectively, in the number of associated trials initiated in 2022. This growing focus on alternative targets highlights the ongoing exploration of more personalized and potentially more effective treatment approaches for cancer patients.

Interestingly, melanoma remains the primary focus across all indications for IO trials. This reflects the significant success of IO therapies in treating this aggressive form of skin cancer.

B) Diagnostics

Diagnostic devices have become a game-changer in the field of oncology. Their ability to facilitate early detection, accurate diagnosis, and the development of personalized treatment plans has fundamentally transformed how we approach cancer care. This revolution is driven by two key trends: the increasing importance of companion diagnostics and the growing use of predictive biomarkers.

Companion diagnostics are specialized tests designed to identify specific patient subpopulations that are most likely to benefit from a particular therapy. These tests often focus on identifying genetic mutations or biomarkers that indicate a patient's susceptibility to a specific cancer drug. With the rise of advanced therapies targeting unique genetic profiles, the demand for companion diagnostics is expected to surge. By 2022, the number of companion diagnostics associated with oncology treatments had already reached a staggering 50. This highlights their crucial role in ensuring patients receive the most effective and targeted treatment options available.

The identification of new biomarkers, such as Trop-2 and CEACAM5, is leading to a phenomenon known as "disease fragmentation" in oncology. This essentially refers to the subcategorization of cancer types based on specific genetic or molecular characteristics. While this may seem like increased complexity, it paves the way for more targeted therapy innovation. By identifying these distinct sub- groups of cancer, researchers can develop therapies specifically tailored to their unique genetic profiles.

- **Liquid Biopsy: coming of age**

Liquid biopsies, a revolutionary technology that analyzes biological fluids like blood for cancer detection and monitoring, have witnessed remarkable progress in recent years. This advancement has not only paved the way for their routine use in clinical settings but also opened exciting possibilities for further research in the fight against cancer.

Unlike traditional tissue biopsies, which involve extracting a small sample of tissue for analysis, liquid biopsies offer a minimally invasive and more patient-friendly approach. This is particularly beneficial for patients who may be too frail or at risk for complications from a traditional biopsy procedure. The ease and safety of liquid biopsies have significantly increased their adoption in clinical practice.

Currently, liquid biopsies see their most widespread use in the diagnosis and monitoring of non-small cell lung cancer (NSCLC). This is largely due to the successful development of tests that can identify specific genetic mutations associated with NSCLC. By analyzing circulating tumor cells (CTCs) or cell-free DNA (cfDNA) in a patient's blood, liquid biopsies can provide valuable insights into the presence and characteristics of the cancer, aiding in diagnosis and guiding treatment decisions.

The research potential of liquid biopsies is vast. Ongoing research is exploring the use of liquid biopsies to monitor treatment response in real-time, allowing for adjustments to be made as needed. Additionally, scientists are investigating the possibility of using liquid biopsies for minimal residual disease (MRD) detection, which involves identifying and eliminating any remaining cancer cells after treatment completion. This holds immense promise for reducing the risk of cancer recurrence.

- **ctDNA**

The concept of liquid biopsy has emerged as a revolutionary tool in the fight against cancer. Unlike traditional tissue biopsies, which require extracting a physical sample of tissue, liquid biopsies offer a

minimally invasive approach. This is particularly valuable in situations where obtaining sufficient or even any tumor tissue may be difficult or even impossible due to the location or size of the tumor, or the patient's health condition.

Liquid biopsies analyze various elements found in bodily fluids, primarily blood. These elements include circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), extracellular vesicles (EVs), and tumor-educated platelets (TEPs). Each element offers unique insights into the presence and characteristics of cancer.

Among these various elements, ctDNA is currently considered to hold the most significant promise for cancer diagnostics in the coming years. ctDNA fragments are shed by tumor cells into the bloodstream, providing a "liquid biopsy" of the tumor itself. Extensive research efforts are currently focused on ctDNA, particularly about lung cancer.

The exploration of ctDNA offers a multitude of exciting possibilities in oncology. One promising application is early cancer detection. By detecting ctDNA fragments even before a tumor becomes large enough to be visualized through traditional methods, liquid biopsies may enable earlier diagnoses and intervention.

One of the most exciting aspects of ctDNA analysis is its ability to monitor tumor burden and treatment response. Since ctDNA levels typically correlate with tumor size, they can serve as a reliable indicator of disease stage. Additionally, changes in ctDNA levels over time can effectively track the progression of the cancer or the effectiveness of a treatment plan. This non-invasive monitoring tool allows doctors to adjust treatment strategies as needed, potentially leading to improved patient outcomes.

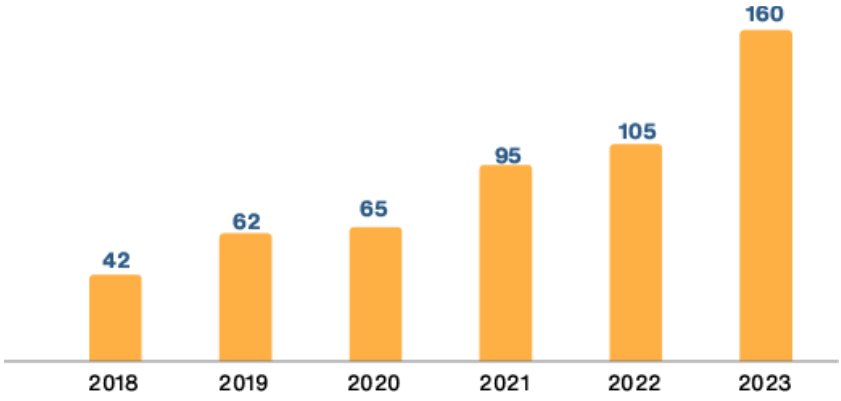

Fig. 12 Number of studies for ctDNA (2018 - Sep 2023)

Source: Cancer compass: Advances, approvals & regulatory updates. Healthark Insights. 20223

5. DISCUSSION

The global oncology drug market, while reaching a substantial USD 169.4 billion, is experiencing a period of transition. Facing increased competition from other therapeutic areas and the looming threat of patent expiration, the market demands continuous innovation. Mergers and acquisitions are on the rise as established players like F. Hoffmann-La Roche Ltd (including Genentech), Bristol Myers Squibb, Pfizer, and Johnson & Johnson solidify their positions.

A shift is underway in research and development focus. Clinical trials for blood cancers are declining, while those for solid tumors are holding steady. This trend reflects a growing interest in exploring cell-based immunotherapies and targeted therapies for aggressive malignancies. The development of sophisticated biomarker screening techniques is paving the way for personalized medicine approaches, allowing clinicians to tailor treatment regimens to a patient's specific tumor profile.

Challenges remain, however, in ensuring wider access to promising treatments like CAR T-cell therapy and optimizing the use of PD-1/PD-L1 inhibitors. The future of oncology holds immense promise. The emergence of antibody-drug conjugates (ADCs), LAG-3 targeted therapies, and mRNA vaccines signifies a new era of possibilities for improved patient outcomes. Notably, emerging biopharma companies are playing a critical role in this progress. These companies now account for a commanding 60% of all clinical trials initiated in oncology, demonstrating a near-doubling of their contribution since 2014.

A particularly noteworthy trend is the rise of mRNA vaccine research within the biotherapeutic pipeline. This surge in interest highlights the potential of utilizing mRNA technology to create personalized and effective cancer vaccines, offering a more precise and potentially less toxic approach compared to traditional therapies.

Key areas of focus:

- Shifting R&D Focus: The decline in blood cancer trials and a corresponding rise in solid tumor trials reflects a strategic reprioritization within the research community.
- Personalized Medicine: Advancements in biomarker screening, particularly next-generation sequencing (NGS) and liquid biopsies, are enabling a new era of personalized medicine in oncology.
- Emerging Therapies: The future of oncology is bright with the ongoing development of next-

generation biotherapeutics, including ADCs, LAG-3 targeted therapies, and mRNA vaccines.

- The Rise of Biopharma Companies: Emerging biopharma companies are playing an increasingly significant role in oncology research, nearly doubling their share of initiated clinical trials since 2014.

6. CONCLUSION

Cancer is a growing global health crisis with a projected rise in new cases to 29 million by 2040. Lung cancer is the most common, followed by breast, colorectal, prostate, and stomach cancers. Breakthroughs in science, mergers and acquisitions, and a focus on targeted therapies are transforming oncology. However, disparities in access to these advancements pose a significant challenge.

The oncology market is witnessing a surge in targeted therapies, leading to increased healthcare spending but offering new hope for patients. Emphasis is shifting towards personalized medicine with drugs tailored to individual cancer profiles. While the overall number of oncology trials remains stable, there's a fascinating trend – a surge in the development of drugs targeting specific antigens like HER2 and Trop-2. Phase II trials for lung, breast, and blood cancers make up a large portion of ongoing research.

Regulatory approval pathways differ geographically, with the US FDA prioritizing breast cancer breakthroughs and the EMA focusing on lung, lymphoma, and myeloma. The past five years have seen advancements in novel modalities like antibody-drug conjugates (ADCs), bispecific antibodies, and radioligand therapies, offering promising treatment options for various cancers. Emerging biopharma companies are driving innovation, sponsoring 60% of oncology trials in 2023, up from 33% a decade ago. Evidence for AI's potential in oncology research is growing, suggesting its role in accelerating candidate drugs to clinical development.

While PD-1/PD-L1 inhibitors remain dominant, new targets beyond these established immune checkpoint molecules are being explored, including LAG-3. The future of oncology is bright with the development of next-generation biotherapeutics, including mRNA vaccines. This personalized approach holds immense promise for improved cancer treatment outcomes.

Overall, the oncology landscape is undergoing a dynamic transformation marked by groundbreaking advancements, targeted therapies, and the pursuit of personalized medicine. However, ensuring equitable access to these innovations alongside continued research into novel treatment modalities remains crucial in the fight against cancer.

7. REFERENCES

1. Clinicaltrials.gov [Internet]. Clinicaltrials.gov. [cited 2024 Jun 20]. Available from: https://clinicaltrials.gov/

2. Oncology regulatory review [Internet]. U.S. Food and Drug Administration. FDA; 2023 [cited 2024 Jun 20]. Available from: https://www.fda.gov/about-fda/2022-oce-annual-report/oncology-regulatory-review

3. Mathur P, Sathishkumar K, Chaturvedi M, Das P, Stephen S. Cancer incidence estimates for 2022 & projection for 2025: Result from National Cancer Registry Programme, India. Indian J Med Res [Internet]. 2022 [cited 2024 Jun 20];156(4):598. Available from: http://dx.doi.org/10.4103/ijmr.ijmr_1821_22

4. Tests and procedures used to diagnose cancer [Internet]. Cancer.gov. 2015 [cited 2024 Jun 20]. Available from: https://www.cancer.gov/about-cancer/diagnosis-staging/diagnosis

5. from: https://www.pharmacompass.com/data-compilation

6. 2022 OCE annual report [Internet]. U.S. Food and Drug Administration. FDA; 2024 [cited 2024 Jun 20]. Available from: https://www.fda.gov/about-fda/oce-annual-reports/2022-oce-annual-report

7. Goldberg P. Contributor spotlight: FDA Oncology Center of Excellence [Internet]. The Cancer Letter. 2023 [cited 2024 Jun 20]. Available from: https://cancerletter.com/in-the-archives/20230324_5/

8. Fiedler K, Lazzaro S, Lutz J, Rauch S, Heidenreich R. mRNA Cancer Vaccines. In: Recent Results in Cancer Research. Cham: Springer International Publishing; 2016. p. 61–85

9. Franklin MR, Platero S, Saini KS, Curigliano G, Anderson S. Immuno-oncology trends: preclinical models, biomarkers, and clinical development. J Immunother Cancer [Internet]. 2022 [cited 2024 Jun 20];10(1):e003231. Available from: https://jitc.bmj.com/content/10/1/e003231

10. Radio Data compilation [Internet]. Pharmacompass.com. [cited 2024 Jun 20]. Available
11. Ipharmacenter.com. [cited 2024 Jun 21]. Available from: https://www.ipharmacenter.com/post/top-selling-cancer-drugs-2022-2023-best-cancer-productsipharmacenter
12. harmacenter.com. [cited 2024 Jun 21]. Available from: https://www.ipharmacenter.com/post/top-selling-cancer-drugs-2022-2023-best-cancer-productsipharmacenter#:~:text=Merck's%20PD%2DL1%20inhibitor%20Keytruda,best%2Dselling%20product%20of%20Merck
13. Fda.gov. [cited 2024 Jun 21]. Available from: https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeuticbiological-products/novel-drug-approvals-2023
14. Zynyz for the treatment of Merkel cell carcinoma, US [Internet]. Clinical Trials Arena. 2023 [cited 2024 Jun 21]. Available from: https://www.clinicaltrialsarena.com/projects/zynyz-treatment-mcc-us/
15. Aptitudehealth.com. [cited 2024 Jun 21]. Available from: https://www.aptitudehealth.com/oncology-news/new-treatment-options-oncology-fda-ema-drugapprovals-q2-2023/
16. Thepharmaletter.com. [cited 2024 Jun 21]. Available from: https://www.thepharmaletter.com/listing/mergers-acquisitions/oncology?tagid[]=32
17. [cited 2024 Jun 21]. Available from: http://file:///C:/Users/ADMIN/Desktop/White-paper_Annual-Pharma-RD-Review-2024.pdf
18. Global oncology trends 2024: Outlook to 2028 [Internet]. Iqvia.com. [cited 2024 Jun 21]. Available from: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-oncology-trends-2024
19. Boni V, Sharma MR, Patnaik A. The resurgence of antibody drug conjugates in cancer therapeutics: Novel targets and payloads. Am Soc Clin Oncol Educ Book [Internet]. 2020 [cited 2024 Jun 21];40(40):e58–74. Available from: https://pubmed.ncbi.nlm.nih.gov/32315240/
20. Jin S, Sun Y, Liang X, Gu X, Ning J, Xu Y, et al. Emerging new therapeutic antibody derivatives for cancer treatment. Signal Transduct Target Ther [Internet]. 2022 [cited 2024 Jun 21];7(1). Available from: https://pubmed.ncbi.nlm.nih.gov/35132063/

21. Fernandez AI, Liu M, Bellizzi A, Brock J, Fadare O, Hanley K, et al. Examination of low ERBB2 protein expression in breast cancer tissue. JAMA Oncol [Internet]. 2022 [cited 2024 Jun 21];8(4):607. Available from: http://dx.doi.org/10.1001/jamaoncol.2021.7239

22. Strengthening pathways for cell and gene therapies: Current state and future scenarios [Internet]. Iqvia.com. [cited 2024 Jun 21]. Available from: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/strengthening-pathways-for-cell-and-gene-therapies

23. IQVIA CAR T-Cell Monitor [Internet]. Iqvia.com. [cited 2024 Jun 21]. Available from: https://www.iqvia.com/library/fact-sheets/iqvia-car-t-cell-monitor

24. Global oncology trends 2023 [Internet]. Iqvia.com. [cited 2024 Jun 21]. Available from: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-oncology-trends-2023

25. Biosimilars in the United States 2023-2027 [Internet]. Iqvia.com. [cited 2024 Jun 21]. Available from: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/biosimilars-in-the-united-states-2023-2027

26. Cancer compass: Advances, approvals & regulatory updates [Internet]. Healthark Insights. 2023 [cited 2024 Jun 21]. Available from: https://healtharkinsights.com/report/cancer-compass-advances-approvals-regulatory-updates/