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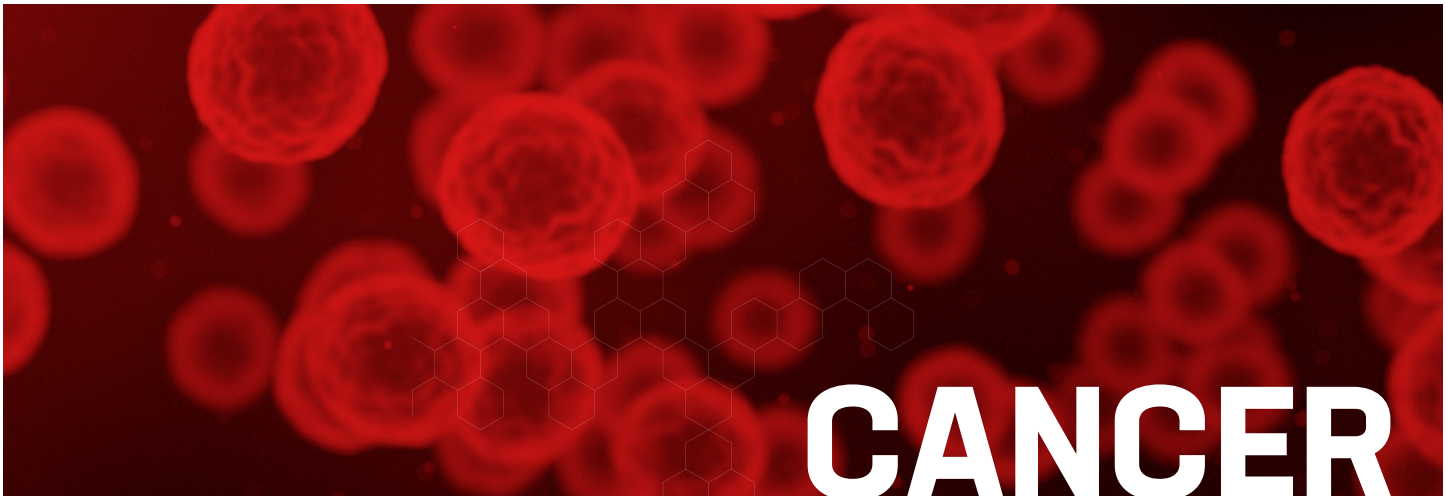
MEDICINES IN DEVELOPMENT FOR CANCER

2023 REPORT



Cancer: A Tale of Two Cities

"We are in a new era of cancer treatments thanks to the transformative power of biopharmaceutical innovation. Today, scientists are working on four medicines to find even better ways to treat kids with neuroblastoma and give more children a chance for a long and healthy life. Researchers are also developing nearly 100 potential medicines to help breast cancer patients who still lack viable options. And recently, the first pediatric patients to receive CAR-T therapy for acute lymphoblastic leukemia are celebrating a decade of being cancer-free.

But eclipsing this era is the looming threat of government price setting. Policies like those included in the Inflation Reduction Act (IRA), in-state prescription drug affordability boards and changes to intellectual property rights can turn back the clock on all the advances in the fight against cancer made over the last several decades. One area I'm particularly concerned about is the way the IRA has a chilling effect on the development of small molecule medicines. Most cancer treatments approved by the FDA are small molecules that come in pill or tablet form. The law introduced a "pill penalty," targeting these medicines with shorter pricing timelines compared to other types of treatments.

Simply put, we are living in a tale of two cities, where it's the best of times on the science side, but the worst of times in terms of the political environment that we're operating in. ***At a time when science has never been more promising, we need our policymakers to prioritize the fight against cancer, not a fight on cures.****"*

– Stephen J. Ubl, President and CEO of PhRMA

1,600 Treatments and Vaccines in Clinical Development for Cancer, More Than Doubling Since 2014

Decades of research unlocking the secrets, nature and origin of cancer have led to an unprecedented amount of targeted treatment approaches and improved prognosis for many cancer patients. A range of game-changing new treatment approaches–such as personalized medicines, CAR-T cell therapies, immune checkpoint inhibitors and many others– have become available to patients with cancer. Biopharmaceutical research companies are working to develop more effective and better tolerated treatments and 1,600 treatments are currently in clinical trials or awaiting review by the U.S. Food and Drug Administration (FDA).[iii] Of the 1,600 treatments and vaccines in development, many are new, while others are approved medicines being studied for new indications/cancer types or expanded to additional patient populations, such as children.

In the last 30 years, new treatment approaches have contributed to significant reductions in mortality and increases in survival that has been made in the fight against cancer. Since peaking in the early 1990s, cancer death rates have declined 33%, leading to more than 3.8 million cancer deaths avoided from 1991 to 2020.[i] Across all cancers, today the chances a cancer patient will live five years or more is 68%, an increase of 39% since 1975.[i] These gains are even more remarkable given that cancer is not just one disease but instead a collection of hundreds of diseases characterized by the growth and spread of abnormal cells.

But while this progress has been significant, there continues to be considerable unmet medical need for many types of cancer, for which there are no treatments or limited treatment options, including rare cancers and hard to treat cancers. Even cancers currently with effective treatments can have subtypes that do not respond to treatment. Additionally, new treatments can potentially address the very real threat of tumor recurrence. Perhaps most importantly, cancer is a constantly evolving treatment paradigm. Likewise, there will always be a need for new treatments and vaccines that extend survival beyond currently available standards of care or reduce side effects relative to existing therapies.

JUST THE FACTS

Over

1.9 Million

new cases of cancer are estimated to be diagnosed in the U.S. 2023.[i]

33%

decline in U.S. cancer deaths since peaking in 1991[i]

1.3 million

prevented deaths associated with new cancer treatments[ii]

More than

18 million

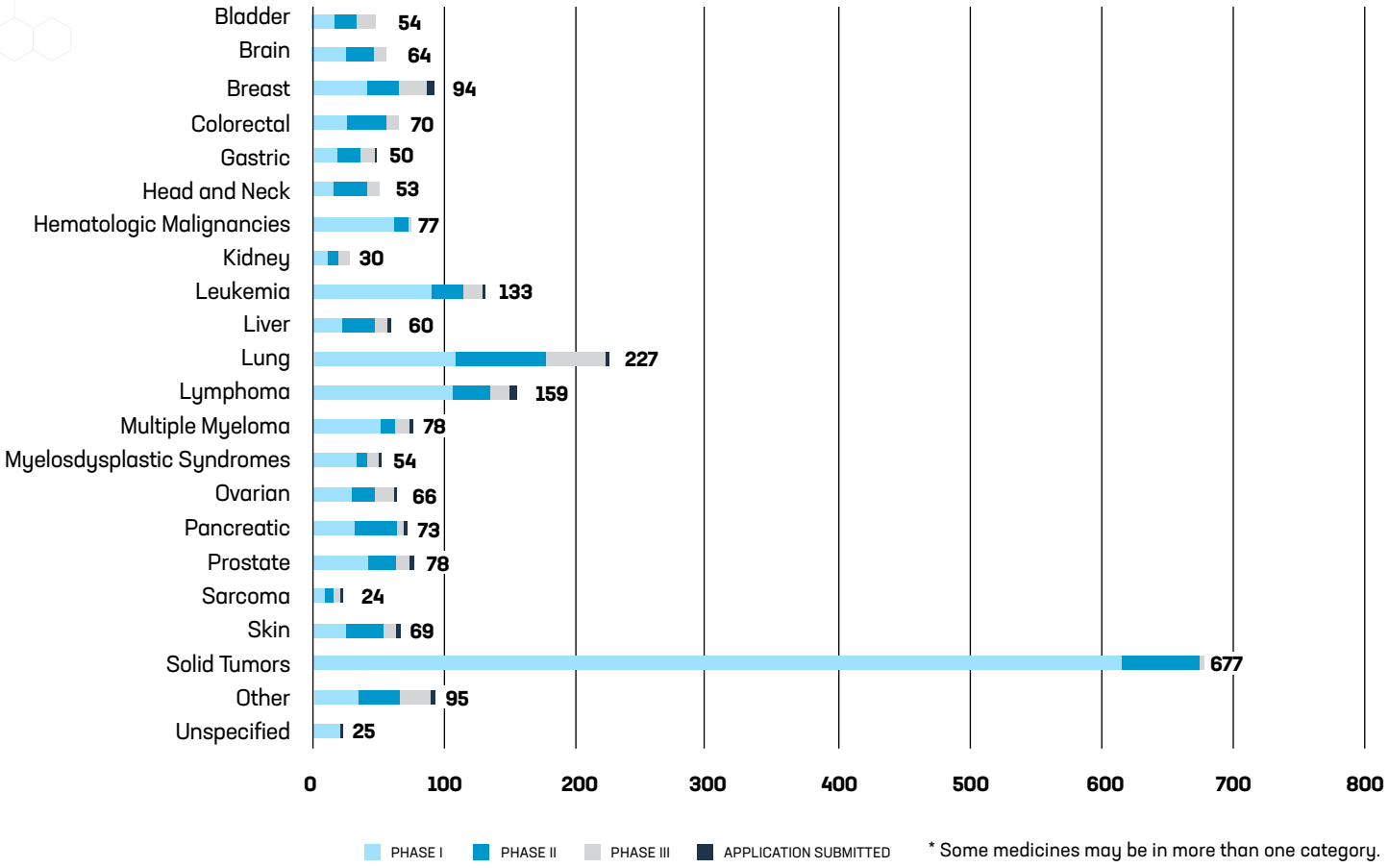
Americans are cancer survivors (as of January 2022)[i]

The medicines in development include:

- **133** for several types of leukemia, which account for an estimated 3% of all new cases of cancer in 2023.[i]
- **227** for lung cancer, for which an estimated 238,340 new cases and 127,070 deaths are expected in 2023.[i]
- **159** for lymphoma, including Hodgkin's lymphoma and non-Hodgkin's lymphoma, which accounts for an estimated 4.6% of all new cancer diagnoses in 2023.[i]
- **94** for breast cancer, the leading cancer diagnosed in women in the U.S. with an estimated 297,790 new cases and 43,170 deaths in women expected in 2023. The breast cancer death rate for females peaked in 1989 and has then declined by 43% (as of 2020).[i]
- **69** for skin cancer, including **63** for melanoma, for which an estimated 97,610 new cases and 7,990 deaths are expected in 2023.[i]
- **78** for prostate cancer, the leading cancer diagnosed in men in the U.S., accounting for nearly 15% of cancer diagnoses expected in 2023. The death rate from prostate cancer has declined by half since its peak in 1993, mainly attributed to earlier detection through prostate-specific antigen (PSA) testing and advances in treatment.[i]
- **78** for multiple myeloma, with an estimated 35,730 new cases being diagnosed in 2023 and 12,590 deaths.[i]
- **73** for pancreatic cancer, for which an estimated 64,050 new cases and 50,550 deaths are expected in 2023.[i]
- **64** for brain tumors, including glioblastoma, the most commonly occurring primary malignant brain tumor, accounting for 50% of all malignant tumors.[iv]
- **70** for colorectal cancer, the third most common cancer among adults, excluding skin cancer. An estimated 153,020 new cases and 52,550 deaths are expected in 2023.[i]
- **66** for ovarian cancer, with an estimated 19,710 new cases being diagnosed in 2023 and 13,270 estimated deaths.[i]
- **60** for liver and bile duct cancer, for which an estimated 41,210 new cases and 29,380 deaths are expected in 2023.[i]
- **50** for gastric cancers, which include stomach cancer, for which an estimated 26,500 new cases and 11,130 deaths are expected in 2023.[i]
- **54** for bladder cancer, for which an estimated 82,290 new cases and 16,710 deaths are expected in 2023.[i]
- **53** for head and neck cancers, including cancers of the throat, mouth, sinuses and the salivary gland, for which an estimated 54,320 new cases and 11,580 deaths in 2023.[i]
- **30** for kidney cancer, one of the 10 most common cancers diagnosed in adults. An estimated 81,800 new cases and 14,890 deaths are expected in 2023.[i]

Additional medicines are in development targeting childhood cancers, sarcomas and other hematologic and solid tumors.

Medicines in Development



* Some medicines may be in more than one category.

Researching Cancer Medicines: Setbacks and Stepping Stones[v]

The more biopharmaceutical researchers discover about the hundreds of diseases that we now know make up cancer, the more complexity and challenges are uncovered. As a result, the process is fraught with many setbacks. For every medicine that successfully makes it to patients, there are many more investigational medicines that do not. But these so called "failures," or setbacks, inform future avenues for research and development and pave the way for new therapeutic options and potential treatment combinations.

An analysis of nine different cancers - malignant melanoma, brain cancer, acute myeloid leukemia, kidney cancer, liver cancer, lung cancer, pancreatic cancer, ovarian cancer and prostate cancer - shows just how challenging the process can be. Since 1998, there have been 1,315 unsuccessful attempts for medicines seeking FDA approval compared to only 111 which were ultimately approved.

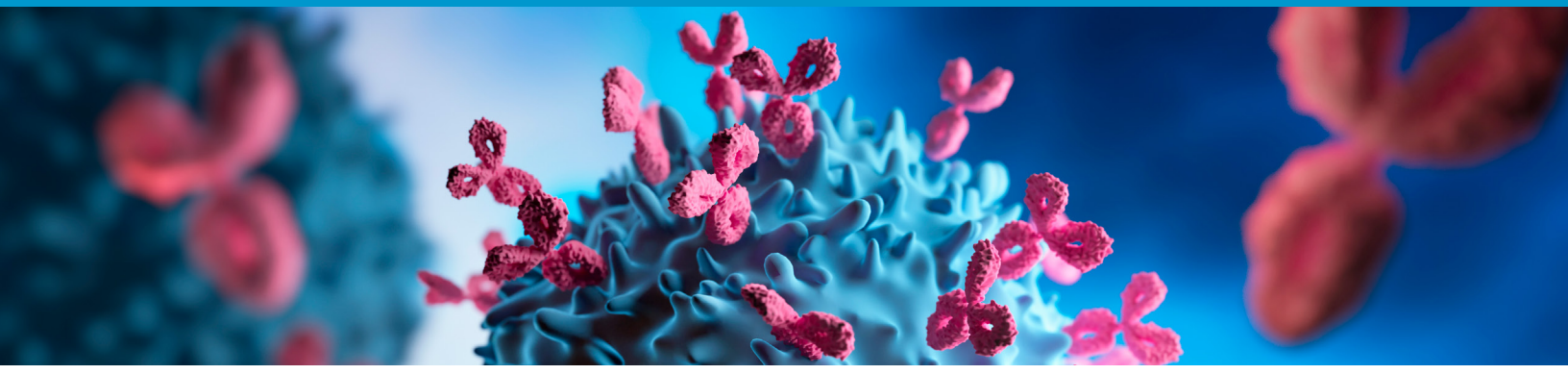
The complexity of cancer is reflected in the drug development process. Researchers face many unique and daunting challenges in developing medicines to treat the myriad forms of cancer, as they often find ways to evade the immune system and mutate to resist treatments. Researchers continue to face substantial scientific challenges in the pursuit of new cancer medicines for many reasons. For example:

Complex Biological Environment	Cancers Are Very Adaptive	Biological Drivers May Vary
Researchers must examine the complex biological environment within which the tumor exists. Gene mutations, immune system response, and external environmental factors all contribute to the complexity of the disease.	A drug may target a key protein involved in the disease, but the cancer may in turn respond by finding a new pathway to continue its spread.	Even within a given tumor, the biologic drivers (e.g., genetic mutations, gene expression) of the cancer can vary from cell to cell. This tumor heterogeneity adds to the complexities of cancer detailed above.

More sophisticated tools are needed to characterize the diversity of the cancer cells found within a single tumor to inform development of new medicines, enable more accurate diagnosis, combat cancer drug resistance and ensure that patients receive the medicine most likely to work for them.

Additional challenges exist that are specific to clinical development. Because cancers are complex and life-threatening diseases, investigational therapies are usually administered only to those patients where standard therapy has failed, or other treatment options have been exhausted. Only after approval and real-world use will most medicines be evaluated in earlier stages of disease progression. Similarly, cancer medicines often work best in combination with other drugs but testing all possible drug combinations is impossible to do in clinical studies.

Therefore, even after initial FDA approval, research continues throughout the lifecycle of each medicine to fully understand the medicine's effects and possibility for future disease impact. The nature of oncology clinical research often leads to cumulative progress over time. The approval by FDA of a new therapy is a significant milestone for patients, but it is often only the beginning. Our knowledge of the full benefits of a therapy emerges over time, through continued research and real-world clinical practice. While many of the medicines in development may represent critical first-time treatments for patients with a range of different cancers, these approvals may represent just the beginning. Only after additional research on cancer medicines--often many years after initial approval--can new clinical data reveal the full value a therapy can bring to patients. Post-approval R&D often leads to new uses for different forms of cancer or different patient populations. It may also lead to approvals for use in earlier treatment line or disease stage, or in combination with other therapies after demonstrating greater treatment benefits than single therapy alone.



Addressing Unmet Patient Needs

While significant progress has been made in the fight against cancer, many of the difficult-to-treat and rare forms of cancer are still in need of new and better treatment options. These cancers are harder to treat, and some are associated with a poorer prognosis. For instance, rare cancers remain hard to understand, partly because they are diverse with fewer patients to study; the biology of some cancer types is difficult to study and understand, making progress to develop new treatments very challenging; childhood cancers are not the same as adult cancers, and they need to be treated differently; and any tumor which has spread is often harder to treat and is associated with a lower survival rate. For these reasons, many cancers represent a significant area of unmet medical need. Examples of types of unmet need in cancer may include:

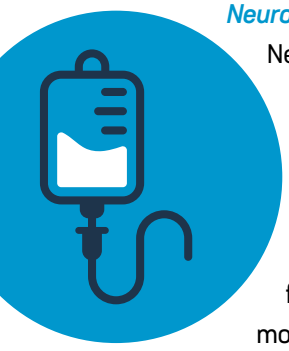
Early Treatment

Late-stage cancer can be less responsive to treatment and make the patient's immune system extremely weak, decreasing a patient's quality of life. Early treatment makes a difference. In early stages, cancer may be more responsive to treatment and the patient's immune system may be able to play a bigger role in helping treatment response. This can make a big difference in a patient's response to treatment. For example, lung cancer is responsible for about one in five of all U.S. cancer deaths. If caught in its early stages, the five-year survival rate is 56%; in its late stages, that number drops to just 5%.[vi]

Immunotherapy, which works with the body's immune system to help fight cancer, has been used in metastatic cancers where it has been proven to extend lives. It could also offer benefits in earlier stages of cancer, where it may be more responsive to treatment, meeting more cancer patients' needs. There is also more research looking at the surgical removal of a tumor supplemented with the appropriate use of immunotherapy.

Glioblastoma

Glioblastoma multiforme (GBM) is the most common and aggressive form of brain cancer in adults. Patients with GBM have an average lifespan of 11-15 months after diagnosis and a 5-year survival rate of 5-19% depending on age.[vii] Progress in the form of innovative medicines has been slow for brain cancer leaving a critical need for continued research and new approaches. The blood-brain barrier makes treating brain cancer difficult, highlighting the importance of the unique capabilities and potential application of small molecule medicines in this form of cancer. The barrier is designed to keep chemicals in the blood from getting into the brain. It limits treatment as this barrier can block anti-cancer drugs from entering the brain to target the tumor.[viii] Treatment for brain tumors is also complicated by the varied mutations and pathways stimulating the tumor growth. Drugs are less able to kill varied cancer cells that are driven by different mechanisms. In addition, therapy-resistant tumor cells can emerge from these diverse cells found within the tumor.[ix] **There are 49 medicines being developed for glioblastoma.[iii]**



Neuroblastoma

Neuroblastoma is a cancerous tumor that occurs when neuroblasts, or immature nerve cells, do not mature into nerve cells and fibers, but rather go on to cause a tumor. It is often diagnosed before age five and can even be diagnosed prior to birth during an ultrasound. Neuroblastoma is the most common cancer among infants younger than one year of age. Approximately 700 to 800 children are diagnosed annually in the U.S. Though low- and intermediate-risk patients are often cured by surgery alone, for high-risk children, 5-year survival has been approximately 50%. Historically, treatment for high-risk neuroblastoma has included surgery, followed by chemotherapy, radiation, or in more severe cases, stem cell transplant. Today, two anti-GD2 monoclonal antibodies have been approved to treat eligible high-risk patients. Both medicines are from a class of immunotherapy that targets GD2, a substance seen in excess on the surface of neuroblastoma cells, allowing the body's immune system to recognize and exclusively destroy the cancer cells. Anti-GD2 therapies in combination therapy with other therapies are becoming a standard of care for eligible patients. This treatment approach has demonstrated improved outcomes with increased survival, providing significant hope for patients and their families. New treatments are needed and research continues on new combinations to bring the potential for extended life to more high-risk children with this devastating disease.[x] **There are 4 medicines being developed for neuroblastoma.[iii]**

Breast Cancer

Breast cancer has many treatments, but there is still unmet medical need for many different types of the disease. For example, metastatic breast cancer remains one of the leading causes of cancer deaths in the U.S. among women and prognosis remains poor. The 5-year survival rate is only 28% compared to 86% to 99% among women with localized or regional breast cancer.[xi] And treatment options for triple-negative breast cancer are more limited because of the lack of therapeutic targets. Additionally, the HER3 protein is expressed in approximately 30% to 50% of breast cancers. This expression is associated with a poor prognosis and is not targeted by any current approved therapies. Early attempts at targeting HER3 were not successful, but new advances are offering some hope.[xii] **There are 94 medicines being developed for breast cancer.[iii]**

Prostate Cancer

Prostate cancer incidence rates are largely impacted by screening with the prostate-specific antigen (PSA) blood test, which mostly detects localized stage disease. From 2007 to 2014, overall incidence of prostate cancer declined sharply coinciding with less PSA testing. Since 2014, however, the rate has increased by 3% per year overall and by about 5% per year for advanced-stage diagnoses. While the prostate cancer death rate declined by half from its peak in 1993 due to earlier detection through PSA testing and advances in treatment, the pace of decline has slowed, likely reflecting the uptick in advanced-stage diagnoses.[i] **There are 78 medicines being developed for prostate cancer.[iii]**

The special needs of cancer patients can be met in a variety of ways:

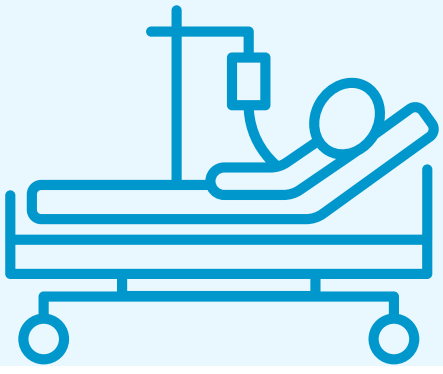
- **Demand for better and less burdensome treatments:** Less burdensome or curative treatments can significantly reduce the burdens associated with a current standard of care, some of which can impose a heavy burden on patients in the form of reduced quality of life, transportation hurdles, caregiver costs and productivity losses.

- **Having a subtype of a disease:** Diseases are not uniform. For example, as more is learned about the role genetic changes play in the development of cancer the more unique subpopulations are identified. For example, while there are existing treatments for lung cancer, without treatments capable of targeting specific genetic mutations associated with rarer lung cancer subtypes, many patients may be left behind.

- **Lack of response to existing treatments:** Patient response can also vary widely due to underlying differences in biology or a range of other factors. For these patients, lacking alternatives can mean having no treatment option at all.

- **Lack of tolerability to existing treatments:** Medications can be associated with side effects, and these can vary widely across individuals. For example, many cancer patients experience varying degrees of side effects due to chemotherapy–both short-term and long-term–but others experience very few. Treatment options that are more tolerable can also reduce barriers to adhering to prescribed treatment regimens.

- **Development of Treatment Resistance:** An individual's cancer can often adapt in ways that make them resistant to existing treatment enabling cancer to grow and spread. Combating treatment resistance is a constant battle for many forms of cancer.



Small Molecules and Biologics: Why We Need Both

The majority of cancer medicines come in two different forms which each bring unique benefits based on the way they interact with cancer cells in the body. Each of these medicine types are essential components of the cancer treatment arsenal as they provide the tools necessary to target the distinct mechanisms involved in the many different diseases collectively known as cancer.

Small molecule medicines, which represent the majority of cancer medicines[xiii], typically come in the form of a tablet or capsule, are taken by mouth and contain a single chemically synthesized active ingredient. Due to their size, small molecules can more easily reach therapeutic targets inside of cells, cross the blood-brain barrier, and are often available in oral dosage forms which offer greater flexibility and convenience in their administration and ultimately reduce barriers to treatment adherence and factors that can drive health disparities.

For cancer specifically, targeted small molecule therapies can act upon specific proteins or genetic material inside cancer cells, causing cancer cells to die.[xiv] As more has been discovered about the genetic changes that lead to the development of various types of cancer, researchers have been able to design therapies capable of targeting these mechanisms. Given cancer begins with genetic changes occurring inside cells, targeted small molecule medicines provide an essential tool in combating the cause of cancer.

Examples of small molecules currently in development are a medicine that targets and degrades estrogen proteins that drive common subtypes of breast cancer and a medicine that promotes cancer cell death in head and neck cancer.

Biologics, also referred to as large molecule medicines, in contrast are made by or from living cells, are structurally complex and are generally administered in a doctor's office or hospital setting via injection or infusion. Due to their larger size, biologics are generally unable to enter cells, but rather are designed to reach therapeutic targets on the surface of cells. For example, monoclonal antibodies, a common form of biologic targeted therapy, are immune system proteins created in the lab to interact with specific targets found on cells, such as cancer cells.[xv] An increasing understanding of the complex ways in which a patient's immune system can interact with cancer cells has led to the development of groundbreaking new treatments that enlist the immune system to fight cancer.

Examples of biologics currently in development include an antibody drug conjugate that combines a monoclonal antibody with an anticancer drug (small molecule) to disrupt cancer cell replication, a monoclonal antibody that activates the immune system to attack and kill cancer cell and cell therapies that target several types of cancer.

Together, these two types of medicines offer patients and health care providers a wide choice of treatment options that are needed and are indispensable in the treatment arsenal against cancer.

Cancer Medicines in Development, Breakdown by Type

Biologics
(including vaccines)

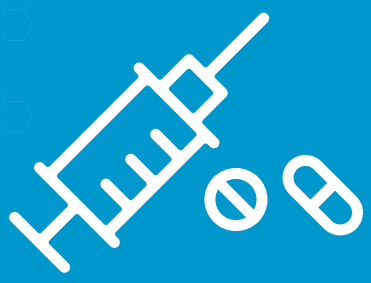
879

Small Molecules

684

Other and Undefined Mechanism

37



New Approaches in Treatment Find Success

Much of the progress in cancer survival is due, in part, to advances in molecular and genomic research that have revealed the unique complexities of cancer and changed our understanding of the disease. Today, scientists recognize that no two cancers are alike; cancer is far more complex and varied. Just as each person's genetic material is unique to them, every patient's cancer is impacted and driven by a variety of unique factors. The condition broadly referred to as cancer is in fact a group of hundreds of different diseases.

Scientific advances have expanded our knowledge of how cancer develops and how to target medicines for specific cancer types, which has resulted in new, more effective therapies for patients. In fact, an average of 85% of medicines in the oncology pipeline are likely to be first-in-class medicines, meaning they use a new and unique mechanism for treating a disease.[xvi] This includes 79% of medicines in the clinical research phase that may be first-in-class medicines.[xvii]

Examples of the exciting science behind potential new cancer treatments include:

Adoptive Cell Therapy

White blood cells, called T-cells, play a role in many cancer immunotherapy approaches. In healthy individuals, T-cells identify and kill infected or abnormal cells, including cancer cells. Two promising technologies in development that activate a patient's own T-cells to attack cancer cells are genetically modified chimeric antigen receptor T-cell therapy (CAR-T) and non-genetically modified T-cell receptors (TCR) therapy. Other types of adoptive cell therapy include tumor infiltrating-lymphocytes (TILs) and natural killer cells. **About 8% of the medicines in development use adoptive cell therapies.**

CAR-T therapy is intended to permanently alter a patient's T-cells to multiply in the body and fight the root cause of disease. For treatment, a patient's blood is filtered to remove a population of T-cells, which are then altered in the lab by inserting a gene that produces T-cell surface proteins that can bind cancer cells. The T-cells are then returned to the patient intravenously, where they can then identify and target cancer cells.

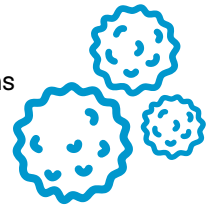
Antibody Drug Conjugates

Antibody-drug conjugates (ADCs) are monoclonal antibodies linked to a therapeutic cytotoxic drug. Monoclonal antibodies can be designed to be highly selective for tumor-associated antigens, allowing them to target specific cancer cells without harming normal or healthy cells. Because improved targeting leaves more healthy cells unharmed, ADCs have the potential to cause fewer side effects than traditional chemotherapy, providing patients with a higher quality of life. When combined with a cytotoxic drug, the antibody binds to specific cancer cells and this antibody-drug combination is taken up by the cancer cells, releasing the cytotoxic drug and causing cancer cell death. **About 6% of the medicines in development are antibody drug conjugates.**

Gene Editing

Gene editing is a technique involving the alteration of genes to correct mutations, introduce new genetic information or remove specific DNA sequences. In gene editing, DNA sections are inserted, replaced, removed, or modified at particular locations in the human genome in order to treat a specific cancer. **Less than 1% of the medicines in development involve gene editing techniques.**

Immune Checkpoint Modulators



The body's immune system includes many checks and balances to protect the body from invading pathogens while preventing itself from inadvertently attacking normal cells in the body. The immune system uses "checkpoint" proteins to either activate or prevent an immune response. Years of research have revealed that some tumors have high levels of proteins that put the brakes on the immune system, preventing it from attacking cancer cells. Since this discovery, researchers have worked to understand the role of these checkpoint proteins and to target them to "release the brakes" on the immune system. **About 5% of the medicines in development are immune checkpoint modulators.**

Metabolic Immunotherapy

Immuno-oncology therapies use many different pathways to activate the body's immune system to attack cancer cells. Metabolic immuno-oncology involves using metabolic pathways to improve the immune system's ability to attack cancerous tumors. It is believed that cellular metabolism plays an important role in moderating parts of the immune system. In cancer, tumor cells can deplete nutrients the immune system needs to work correctly and support the development of immunosuppressive metabolites, making it difficult for the immune system to recognize and attack the tumors. Metabolic immuno-oncology hopes to modulate the activity of immune system and enhance its ability to activate an anti-tumor response by targeting key metabolic enzymes.

Personalized Medicine–Diagnosis and More Precise Treatment

The use of diagnostic tools to identify genetic mutations, the presence of specific proteins, or other molecules that relate to the cancer (biomarkers) allows clinicians to assess which medical treatment would be most effective for each individual patient. For example, a greater understanding of the molecular basis of disease has transformed what was known collectively as "disease of the blood" 60 years ago, into about 40 unique types of leukemia and 50 types of lymphoma, opening up new treatment approaches. Recently, treatments approved for melanoma with specific genetic mutations were accompanied by a diagnostic test to determine which patients would benefit from the treatments.

An emerging technology in personalized medicine uses artificial intelligence (AI). For example, AI can help manage the use of chemotherapy drugs and help predict treatment tolerance by patients for an optimal treatment regimen. AI can also match a patient's genetic profile with the most effective treatments for this patient. Personalized medicines have grown from less than 10% of new therapeutic approvals to 34% in 2022.[xvii]

RNA Interference

RNA interference (RNAi) and antisense RNA are relatively new areas of research and capitalize on a pathway that uses DNA sequence to turn the gene off or modify the gene's expression. These therapeutics are not cell or gene therapies, but they do offer a new understanding of how genes are regulated in the body's cells. RNA therapeutics can potentially block the mechanism of disease-causing proteins. **About 1% of the medicines in development use RNA interference.**

Tumor Agnostic Therapy

Tumor agnostic therapies are treatments for tumors based on a specific genetic mutation or molecular structure, regardless of the cancer type or where it started in the body. This approach provides a new way of thinking about treating patients that is quite different than how treatment plans were developed in the past and provides hope to patients across a wide range of cancers. The first tumor agnostic therapy was approved in 2017, and to date, the FDA has approved six therapies that are targeted towards a specific genetic change across any cancer. **About 1% of the medicines in development are tumor agnostic therapies.**[xviii]

Vaccines

Cancer vaccines are a form of cancer immunotherapy and are considered biological response modifiers. These modifiers work

by either stimulating or restoring the immune system's ability to fight infection and disease. Cancer vaccines can either be preventive, which are intended to prevent cancer from developing in healthy people or meant to treat cancer by strengthening the body's natural immune response against the cancer (called therapeutic vaccines). Currently available preventive vaccines for cervical and other forms of cancer help protect against strains of the human papillomavirus linked to these forms of cancer. Additionally, there is one therapeutic vaccine available for the treatment of prostate cancer in the United States. **About 4% of the medicines in development are vaccines.**

All categories of medicines described above undergo a comprehensive research and development process to meet rigorous FDA standards for safety and efficacy. Comprehensive research into cancers and potential treatments, alongside advances in manufacturing these complex treatments, have positioned the biopharmaceutical industry to continue the great progress made in the treatment of these diseases.

The Patient Perspective

"Watching my loved ones face a cancer diagnosis gave me a deeper appreciation for the need to protect biopharmaceutical research. Every day, families are hoping for new cures or treatment solutions, and it is critical that policymakers pass measures that support these efforts." **– Garian C., Michigan**

"It is critical biopharmaceutical scientists and researchers have the resources they need to research and develop new cancer advancements. As a triple negative metastatic breast cancer survivor, I can tell you without hesitation that the blessing of medical innovation is the only reason I am here today." **– Maura B., Nevada**

"At 40 years old, I faced a serious colon cancer diagnosis. But thanks to new treatment options discovered by the biopharmaceutical industry, I am grateful to say I have been cancer free for the last 25 years. I can't stress enough how important it is to protect medical research and ensure the next generation has access to life-saving cancer medicines." **– Terry U., Ohio**

Spotlight Innovative Medicines in the Pipeline

- An anti-TIGIT monoclonal antibody (mAB) is in development for **non-small cell lung cancer** and **esophageal cancer**. The medicine works as an immune amplifier, by potentially enhancing the body's immune response. It blocks the interaction of TIGIT with a poliovirus receptor that can suppress the body's immune response. It is being studied as a monotherapy and in combination with Tecentriq® (atezolizumab), an approved anti-PD-L1 mAb. The combination of the TIGIT mAb and the PD-L1 mAb offers a dual blockade that has the potential to increase anti-tumor activity.

- An estrogen receptor protein degrader is in development for estrogen receptor positive (ER+)/human epidermal growth factor receptor 2 negative (HER2-) metastatic **breast cancer**. The estrogen receptor is a primary driver of hormone receptor positive (HR+) breast cancer, the most common subtype of breast cancer. The potential treatment is designed to specifically target and degrade the estrogen receptor. It is being developed as a monotherapy and in combination with other therapies.

- An oral small molecule treatment is in development for **head and neck squamous** cell carcinoma. It is designed to promote apoptosis (programmed cell death) in tumor cells by blocking the activity of at least three inhibitors of apoptosis proteins (IAPs). IAPs are key inhibitors of the process that activates enzymes called caspases that contribute to the breakdown of cancer cells. The potential treatment binds to the IAP and prevents it from inhibiting caspase activation leading to cancer cell destruction.

- A fixed-dose combination treatment of two approved medicines is in development for metastatic castration resistant **prostate cancer** with BRCA mutations. The dual action medicine, in combination with prednisone, targets two drivers of prostate cancer – the androgen receptor and BRCA mutations. The medicine inhibits the production of androgens, which are necessary for prostate cancer growth, and inhibits PARP enzymes, which play a role in DNA repair (in this case specifically the BRCA mutation) that results in tumor cell death. BRCA1 and 2 are tumor suppressor genes and when they work normally, they help keep certain cancer cells from growing and dividing.

Sources:

[i] American Cancer Society, Cancer Facts and Figures 2023

[ii] JP MacEwan et al, "Changes in mortality associated with cancer drug approvals in the United States from 2000 to 2016," J of Med Econ, Nov. 2020

[iii] Number of medicines obtained through public, government and industry sources, and the Adis "R&D Insight" database; current as of October 21, 2023. The medicines referenced in this report include medicines being developed by U.S.-based companies conducting trials in the United States and abroad, PhRMA-member companies conducting trials in the United States and abroad, and foreign companies conducting clinical trials in the United States. Some products may not be in active clinical trials. The information may not be comprehensive.

[iv] National Brain Tumor Society

[v] https://phrma.org/-/media/Project/PhRMA/PhRMA-Org/PhRMA-Org/PDF/P-R/PhRma_Cancer_Research_7142020.pdf

[vi] Late stage cancers on the rise after pandemic delayed screenings (statnews.com)

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