



JUST THE FACTS¹

1.8 M

ESTIMATED NUMBER OF U.S. NEW CASES OF CANCER IN 2020

29%

DECLINE IN U.S. CANCER DEATHS SINCE 1991

42%

OF NEW CANCER CASES ARE RELATED TO PREVENTABLE CAUSES

MORE THAN

16.9 M

AMERICANS ARE CANCER SURVIVORS

MEDICINES IN DEVELOPMENT | 2020 REPORT

CANCER

More Than **1,300** Medicines and Vaccines in Clinical Testing for Cancer

In the last 30 years, significant progress has been made in the fight against cancer. Since peaking in 1991, cancer death rates have declined 29%, leading to more than 2.9 million cancer deaths avoided.¹ The most recent data show that between 2016 and 2017 alone, death rates declined by 2.2%, the largest single-year drop ever recorded.² Accordingly, rates of cancer survivorship also continue to rise. The number of cancer survivors living in the United States has increased from three million in 1971 to 16.9 million as of January 1, 2019.¹

Approximately 73% of survival gains in cancer are attributable to treatment advances including new medicines.³ Between 1988 and 2000, advances in treatment for cancer have saved 23 million years of life and added \$1.9 trillion to society based on improved productivity, extended life and other factors.⁴

While meaningful progress has been and continues to be made against cancer, it is still the second leading cause of death in the United States, accounting for 21% of all deaths.⁵ As 2020 comes to a close, it is estimated that more than 1.8 million new cancer cases will be diagnosed and more than 606,000 Americans will die from cancer this year alone (more than 1,600 people per day).¹ (Note: These estimates are prior to COVID-19. The pandemic has impacted treatment access and cancer screenings and may impact these estimates.)

With cancer cases expected to increase, the demand for cancer prevention, screening and treatment services as well as the overall costs to care for the growing number of patients are projected to dramatically increase.⁶ Today, the direct medical costs of cancer care are estimated at \$80.2 billion in the U.S. annually. And the indirect costs of lost productivity each year due to cancer-related mortality include \$94.4 billion in lost earnings.⁷ With cancer incidence expected to increase, these costs underscore not only the need for new treatments to address substantial unmet medical needs, but for earlier diagnosis and treatment to head off these costs and lead to longer and healthier lives in the years ahead.

To continue the progress and deliver hope to those battling cancer, biopharmaceutical research companies are working to develop more effective and better tolerated treatments. Today, **1,361** medicines and vaccines for various cancers are currently in development by innovative biopharmaceutical research companies, all of which are in clinical trials or awaiting review by the U.S. Food and Drug Administration (FDA).⁸ The medicines in development include:

- **145** for several types of leukemia, which account for more than three percent of all new cases of cancer.¹
- **141** for lung cancer, the leading cause of cancer death in the U.S. with 228,820 new cases and more than 135,000 deaths expected in 2020.¹
- **129** for lymphoma, including non-Hodgkin lymphoma, which account for nearly five percent of all new cancer diagnoses.¹
- **108** for breast cancer, the leading cancer diagnosed in women in the U.S. with more than 279,000 new cases and more than 42,000 deaths expected in 2020. The female breast cancer death rate peaked in 1989, then declined by 40% in 2017.¹
- **85** for prostate cancer, accounting for nearly 11% of cancer diagnoses. The death rate from prostate cancer has declined by 52% since 1993 mainly attributed to earlier detection through Prostate-specific antigen (PSA) testing and advances in treatment.¹
- **72** for multiple myeloma, with an estimated 32,270 new cases being diagnosed in 2020 and 12,830 deaths.¹
- **67** for brain tumors, including gliomas, which represent about 33% of all brain tumors.⁹
- **49** for ovarian cancer, with an estimated 21,750 new cases being diagnosed in 2020 and 13,940 deaths.¹

A robust pipeline of additional medicines and vaccines are in development targeting bladder cancer, colorectal cancer, kidney cancer, pancreatic cancer, skin cancer, stomach cancer, childhood cancers and other solid tumors.

While a particular type of cancer has historically been classified based on the tissue in which the cancer cells first began to develop, researchers are working to more precisely and accurately define cancers based on cellular and molecular characteristics. The ability to identify particular cancers in scientifically and clinically meaningful ways lays the groundwork for the hurdle ahead: researching and developing new medicines that will be safe and effective in treating those cancers.

For some cancers, the basic scientific understanding of their root causes provides researchers with better targets for discovering and developing medicines, particularly in cases when the disease is associated with a single gene mutation or known set of mutations. For example, a mutation in the BRAF gene is found in about 50-60% of all cases of cutaneous melanoma.¹⁰ For many other cancers, however, advances in scientific knowledge have revealed the redundancy and complexity of the pathways involved. In these cases, a combination of medicines that hit the cancer from different angles will likely be needed as targeting just one molecular driver could allow the cancer to develop resistance. This is just one example of why the development of effective medicines is extremely challenging.

While there has been enormous progress in understanding many cancers and the underlying biology which drive them, we have also learned how much more there is to learn about this remarkably complex set of diseases. The potential for progress has never been greater but realizing that promise is a challenge that requires talented, dedicated researchers.



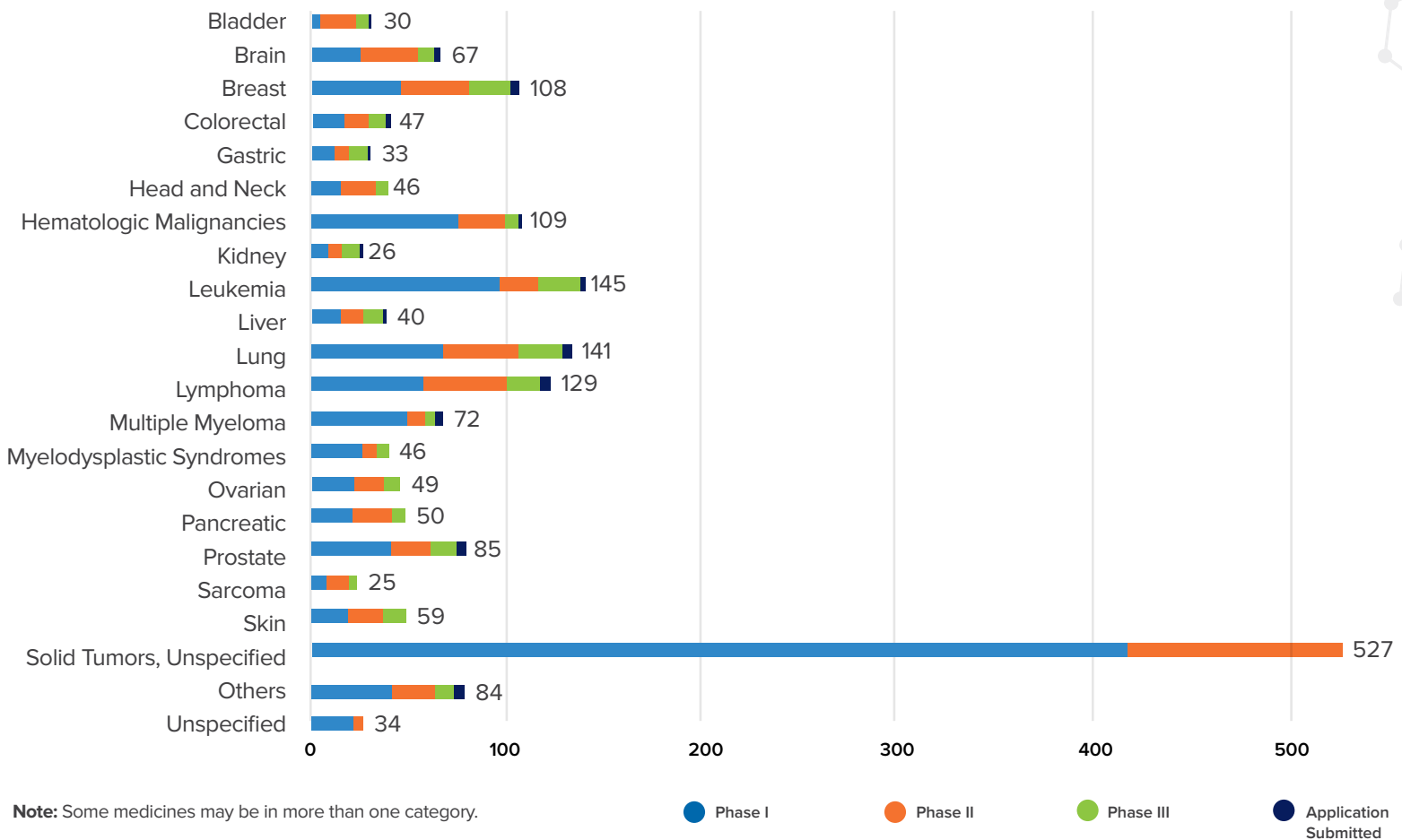
Medicines in the Pipeline

Cancer is not just one disease but instead a collection of hundreds of diseases characterized by the growth and spread of abnormal cells. Researchers are exploring game-changing methods and technologies to fight cancer as well as innovative ways to use existing medicines, either alone or in combination with other therapies. This rapid pace of scientific advances ushered in a new era of medicine for cancer patients over the last decade. Biopharmaceutical researchers' understanding of the underlying biological mechanisms that lead to cancer cell growth create promising avenues for treatment advances. Research into the role of the body's immune system in fighting cancer has yielded some of the most exciting advances, resulting in a new wave of immunotherapies that specifically target cancers. Some of the exciting new medicines in the pipeline include:

- A CD19-directed (a biomarker commonly found on leukemia and lymphoma B-cells) CAR-T cell therapy is in development for relapsed or refractory large B-cell lymphoma, including diffuse **large B-cell lymphoma**. CAR-T cell therapy is a type of immunotherapy where a patient's own T-cells are collected and engineered in the lab to recognize and kill cancer cells. The engineered T-cells are then returned to the patient to treat the cancer. The T-cells in this treatment are modified to recognize and kill malignant B-cells with the protein CD19 on the surface.
- A therapeutic vaccine for **non-small cell lung cancer** (NSCLC) which uses messenger RNA (mRNA) to mobilize the patient's own immune system to fight the tumor(s). mRNA is the cell's blueprint to make proteins and subsequently send them to various parts of the body. mRNA medicines take advantage of the body's biological processes to create a desired therapeutic effect. The vaccine in development targets six specific tumor-associated antigens (substances produced in tumors that trigger an immune response) that are overexpressed in lung cancer. It is being studied in combination with cancer immunotherapy.
- A first-in-class treatment in development for higher-risk **myelodysplastic syndromes** (HR-MDS) targets the NEDD-8 activating enzyme (NAE). Inhibiting the NAE enzyme blocks the modification of select proteins, resulting in disruption of the cell cycle progression and cell survival, leading to cancer cell death. In clinical trials, the medicine used in combination with other anticancer therapies demonstrated promising clinical activity. If approved, it would be the first new treatment for HR-MDS in more than a decade.
- A second-generation CAR-T cell therapy comprised of genetically-modified T cells is designed to target B-cell maturation antigen (BCMA) and to redirect the T-cells to recognize and kill malignant **myeloma** cells. BCMA is a surface protein that is absent in most normal tissues but found in normal plasma cells and the majority of multiple myeloma cells.
- A potential treatment for **bladder cancer, renal cell carcinoma** and **melanoma**, among others, is designed to stimulate cancer killing cells in the body by targeting CD122 on the surface of the immune cells. This experimental immunotherapy is being studied in combination with an approved immune checkpoint inhibitor which works by unleashing the body's own powerful immune system to target and kill cancer cells. The treatment works by increasing the number of tumor-infiltrating lymphocytes (TILs) which generate an immune response leading to increased therapeutic activity of the checkpoint inhibitor to attack cancer cells while leaving normal cells alone.



Medicines and Vaccines in Development for Cancer by Type



The Full Impact of New Cancer Medicines Accumulates Over Time

Post-approval research on existing medicines and new uses is particularly important in cancer treatment and has yielded critical information about the full impact of certain cancer treatments. For example, an initial approval indicating seemingly small improvements in overall survival rates, after longer term study, may be found to result in longer survival rates and/or may find fewer side effects compared to other treatments. Additionally, the initial approval of a novel cancer medicine is a significant milestone for many patients, but it is often just the beginning as researchers continue to explore the effectiveness of treatment in other forms of cancer or in combination with other cancer therapies through continued clinical trials and real-world clinical practice. Demonstrating the importance of expanded uses of existing cancer medicines, the American Association of Cancer Research reports that while the FDA approved 18 new cancer treatments in 2018, they also expanded approvals for 10 previously approved cancer treatments. These expanded approvals can include approvals in different stages of disease or different types of cancer. These subsequent approved uses following clinical trials of existing medicines are often first-time treatments or even breakthrough options for many cancer patients.

As one example, a PD1 checkpoint inhibitor, initially approved to treat metastatic melanoma in 2014, has subsequently been found effective in treating a wide range of cancers in adults and children. In the span of just 6 years, post-approval research led to new indications for the treatment of 13 different cancers. In many of these cancers, approvals were based on clinical trial results which showed the checkpoint inhibitor improved overall progression-free survival. The medicine later became the first cancer treatment approved based on the genetic composition of a tumor regardless of where the tumor originated in the body. This year, the medicine also obtained a second so called “tissue agnostic” approval, thus enabling treatment across an even wider range of cancers and in many cases providing treatment options for patients who previously had none.¹¹

Subsequent approvals which expand the use of cancer medicines alongside other treatments are also extremely valuable. For many cancers, continued exploration post-approval of combinations with different cancer medicines often significantly improves treatment outcomes. New uses for approved medicines require extensive clinical trial data which can lead to fewer side effects, less frequent dosing, new indications, new patient populations and alternative delivery options.

For example, a range of checkpoint inhibitors as well as personalized medicines known as BRAF inhibitors and MEK inhibitors were initially approved to treat metastatic melanoma beginning in 2011 and through additional clinical trials have been proven effective in different stages of melanoma and in combination both within and across these classes. In 2015, the FDA approved the use of two of checkpoint inhibitors in combination as a first-line treatment for some patients with metastatic melanoma after clinical trials showed that 60% of patients responded to the combination compared with 11% who responded to monotherapy.¹³ Similarly, in 2018 the FDA approved two different combinations of BRAF and MEK inhibitors for metastatic melanoma patients. Just this year a triple combination treatment, including a checkpoint inhibitor and a BRAF and MEK inhibitor, was approved for certain metastatic melanoma patients after demonstrating 15 months of progression-free survival in patients.¹⁴

Long-term data has revealed tremendous survival outcomes in advanced melanoma, with 40 percent of patients alive three years after starting treatment with a checkpoint modulator in a recent study.¹⁵ Before the arrival of the first immunotherapy in 2011, survival for these patients was measured in months.

Success of clinical trials following the original approval is not guaranteed. There is tremendous risk and unpredictability in testing a previously approved medicine in a new population or new indication. Biopharmaceutical companies often invest time and resources only to experience devastating late phase failures. Intellectual property protection and other incentives help enable companies to take on the risk and explore a medicine beyond the original indication.

Innovation Comes in Many Forms

For many cancer patients, additional research and development following initial FDA approval leading to new formulations and fewer administrations can result in reduced side effects, increased compliance with the treatment regimen and/or provide greater convenience or quality of life.

Continued innovation that enables delivery of a medicine via a different route provides tremendous value to cancer patients who are often undergoing chemotherapy and require frequent and burdensome infusions. For example, in 2019 the FDA approved a subcutaneous (under the skin) injection formulation of a common treatment for certain HER2-positive breast cancer which was previously administered via infusion. This new formulation includes the same monoclonal antibody as the intravenous treatment along with a recombinant enzyme which enables the delivery of the treatment under the skin. The new formulation delivered via injection can be administered in 2 to 5 minutes, compared to 30 to 90 minutes for the intravenous version allowing less time in the clinic and more comfortable administration for patients.¹⁶

Likewise, continued research and development that results in safe and effective combinations of multiple medicines that may be part of the same treatment protocol or regimen into a single dosage form may significantly reduce treatment burden. For a cancer patient with often complex treatment regimens, such an innovation can be remarkably valuable. For example, this year the



FDA approved a fixed-dose formulation of two monoclonal antibodies for the treatment of certain HER2-positive breast cancer patients. Relative to the previous infusion of each respective therapy, the new combined formulation can decrease breast cancer treatment from sequential 1 to 2.5-hour intravenous infusions to a single 5-minute injection.¹⁷

Fixed-dose combinations chemically bring medicines together in ways that they cannot be separated, and the effect of the medicines combined are often, synergistic, or more beneficial than the medicines separately.¹⁸ Combination medicines are difficult to engineer requiring significant research and testing to ensure each individual medicine in the combination is delivered in the proper dosage and released at the same time. This strategy is often incentivized by patents and represents new and novel formulations which are safe and effective compared to the individual products.¹⁹

Continued research and development can also result in new approaches, forms, technologies and systems for delivering medicine to a patient which can simplify treatment protocols and improve quality of life for cancer patients. A long-approved medicine to treat neutropenia (a low white blood cell count that can lead to dangerous infections) in patients undergoing chemotherapy is now available in a single-use prefilled syringe and on-body injector (12 after initial approval). This convenient approach to administration allows health care providers to start administration of the neutropenia treatment on the same day as chemotherapy in appropriate patients. Prior to this new delivery system, patients were required to visit the cancer clinic or hospital the day after chemotherapy to receive their treatment.²⁰

Increasing Diversity in Cancer Clinical Trials

Clinical trials are critical to the development and proof of efficacy for new treatments in all diseases, including cancer. Unfortunately, less than one in 20 adult patients with cancer participate in a clinical trial.²¹ This disparity is even starker for non-white racial and ethnic groups²¹ with data showing that the clinical trial enrollment of these groups has actually decreased over the past 14 years.²² In 2012, only 17% of patients enrolled in industry-sponsored clinical trials were of a racial or ethnic group other than white, despite these groups making up about one-third of the population.²³ One evaluation found that Black participation reached 10% for only two of the 31 cancer drugs studied.²⁴ Clinical trial participants are disproportionately non-Hispanic white men with higher education levels and household incomes.^{21,25}

PhRMA and its member companies are committed to enhancing diverse participation in clinical trials including identifying and addressing potential barriers to enrollment. Working with the FDA, patient advocacy organizations and other stakeholders across the research ecosystem, biopharmaceutical companies collaborate and employ strategies to encourage greater participation in clinical trials. The FDA Reauthorization Act of 2017, Prescription Drug User Fee Act and the 21st Century Cures Act further enable science-based approaches, including the use of innovative clinical trial approaches and incorporation of patient perspectives into drug development to advance the innovation of clinically meaningful products for patients.

In November 2020, PhRMA member companies launched the first ever industry-wide principles on clinical trial diversity.²⁶ These principles build on our commitment to earn trust and address the systemic issues that deter black and brown communities from participating in clinical trials, so that people who want to participate, can.

Three of the primary barriers to diverse clinical trial participation²⁷ include:

- Lack of knowledge. Many patients do not understand what clinical trials are and are not aware of clinical trials as a treatment option.
- Financial constraint. For many, participating in a clinical trial means taking time off work or care-giving to travel to the clinical trial site. Providing appropriate financial support for participation may help address these barriers and increase clinical trial participation.

- Lack of trust. Some patients may not trust medical research due to historical mistreatment of participants, such as those involved in the U.S. Public Health Service Syphilis Study at Tuskegee, 1932-1972. Education of healthcare providers and community outreach to build trust and increase clinical trial awareness can directly help address recruitment, enrollment, and retention of a diverse clinical trial population, while also expand access to investigational treatments for underserved populations.

Biopharmaceutical companies are addressing the systemic challenges and skepticism that keep Black and Brown communities from participating in clinical trials because of historic wrongs. Clinical trials can give people access to potentially lifesaving medicines and high-quality care. Enhancing diversity in clinical trial participation may lead to evidence that better reflects the patients most likely to use the medicine if approved. As an industry, biopharmaceutical research companies are dedicated to earning the trust, and addressing the systemic issues, that prevent Black and Brown communities from enrolling in clinical trials so that people who want to participate, can.

New Approaches in Treatment Find Success

While new medicines have played a key role in cancer survival gains, much of this progress 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.

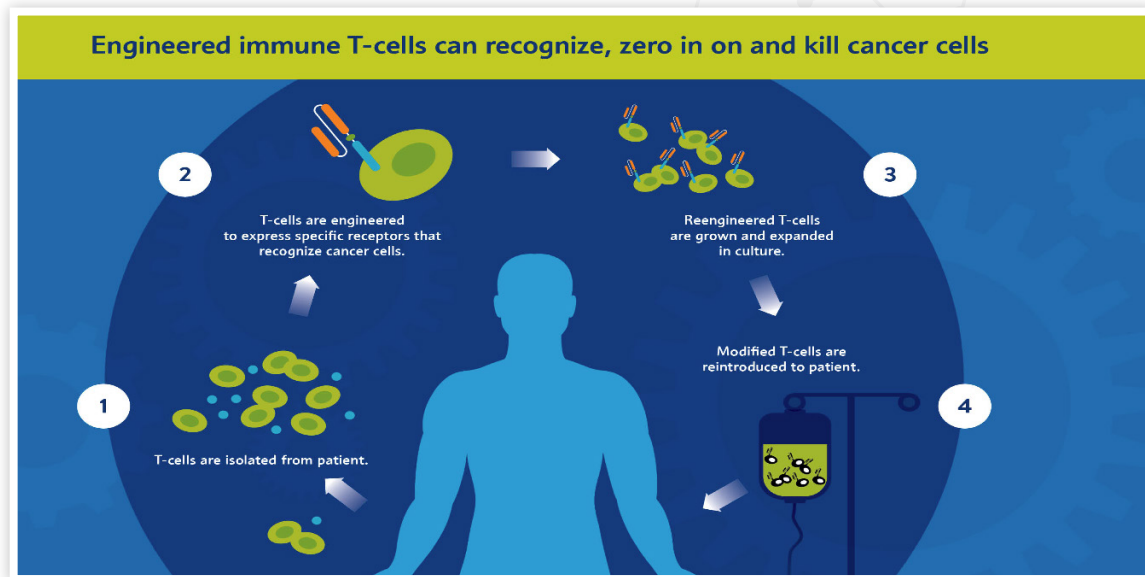
These advances have expanded our knowledge of how cancer develops and how to target medicines for specific cancer types, which has resulted in new, more effective therapies for patients. In fact, an average of 85% of medicines in the oncology pipeline are likely to be first-in-class medicines, meaning they use a new and unique mechanism for treating a disease.²⁸ This includes 79% in the clinical research phase that may be first-in-class medicines.²⁸ 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.

CAR-T therapy is intended to permanently alters a patient's T-cells to multiply in the body into an army to fight the root cause of disease. To receive the 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 targets cancer. The T-cells are then returned to the patient intravenously, where they can then identify and target cancer cells.

CAR-T THERAPY DRIVING BREAKTHROUGHS FOR CANCER PATIENTS



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.

Gene Therapy

Gene therapy seeks to modify or introduce genes into a patient's body with the goal of treating, preventing or potentially curing a disease. Examples of gene therapy approaches include replacing or silencing a mutated gene that causes disease; or introducing a new or modified gene that codes for molecules that block disease into the body.

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.

Immune Checkpoint Modulators

The body's immune system must include 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 in order 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 in order to "release the brakes" on the immune system. Current checkpoint modulators commonly target three proteins – CTLA-4, OX40 and PD-1/PD-L1.



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 enzyme.

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. Targeted medicines have grown from 26% in 2003 to 46% in 2013.²⁹

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.

Tumor Agonistic Therapy

Tumor agnostic therapies are treatments for tumors based 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 provide hope to patients across a wide range of cancers. The first tumor agnostic therapy was approved in May 2017, and to date, the FDA has approved 3 therapies that are targeted towards a specific genetic change across any cancer.

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 cancer helps protect against strains of the human papillomavirus (which is known to cause the disease), and one therapeutic vaccine (for prostate cancer) is approved in the United States.

All of the categories of medicine described above undergo a comprehensive research process in order to meet rigorous FDA standards for safety and efficacy. In addition to carefully conducted pre-clinical and clinical studies, this also includes research to establish robust manufacturing and storage plans, in order to ensure the purity and potency of the therapy. The 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.

Researching Cancer Medicines – Setbacks and Stepping Stones

Novel medicines that target the underlying causes of the disease are improving the outlook for many patients. But behind every medicine that makes it to patients there are many investigational medicines that fail. The biopharmaceutical pipeline includes many of these so-called “failures” which should more appropriately be considered setbacks. The nature of conducting research in areas of high scientific complexity and regulatory uncertainty is that failure is inevitable. The knowledge gained helps to inform future research and development projects, including new therapeutic strategies and potential treatment combinations.

An analysis³⁰ 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 many unsuccessful attempts and also some triumphs with medicines beating the odds and garnering approval by the FDA with **1,315 drug failures and 111 approvals to treat the 9 cancers** examined in the analysis.

These numbers give a sense of the magnitude of the complexities in cancer research and underscore the hurdles inherent in the process, as well as the progress represented by new treatments that emerge from years of research and setbacks. Many of these medicines target the root cause of cancers at the molecular level, some harness the body’s immune system to attack cancer cells, while some work in conjunction with other medicines to unlock new progress.

Brain Cancer

The American Cancer Society estimates about 18,020 adults and children in the U.S. will die this year from brain and spinal cord tumors, and about 23,890 new cases will be diagnosed.¹ Brain cancer treatment and research is complicated by the blood-brain barrier, which is designed to keep chemicals in the blood from getting into the brain, including anti-cancer treatments.

There is significant unmet need for patients with an aggressive form of brain cancer called glioblastoma multiforme (GBM). Researchers are committed to continue in their efforts to research and develop new treatments for GBM, but they have faced significant hurdles. Since 1998, there have only been 3 new drug approvals for GBM, while another 122 medicines have failed in the development process having been discontinued, suspended, or had no development reported.³⁰ That is a 41:1 ratio of unsuccessful attempts to FDA-approved medicines.

Like most cancers, researchers are working to better understand brain tumors at the molecular level, the mutations driving them, the biomarkers that reflect their state, how they interact with the immune system, and how best to treat each patient individually.

Immunotherapies that harness the body’s own powerful ability to kill cancer cells are considered particularly promising. A recent trial for GBM patients tested an immune checkpoint inhibitor and found that when the inhibitor was given to GBM patients before surgery it nearly doubles median survival time (417 days compared with 228 days).³¹

Researchers are also exploring the development of vaccines in the fight against glioblastoma. One study that released promising results in 2019 focused on a therapeutic vaccine in development made from the patient’s own tumor cells designed to help the immune system recognize and attack the tumor. The study showed that the vaccine suspended cancer growth, slowed recurrence, and extended survival.³² In addition, preclinical research has suggested that combining three immunotherapies which work by three different mechanisms may have potential in leading to long-term remission.³³

Acute Myeloid Leukemia (AML)

A flurry of recent approvals for AML followed nearly two decades without major new treatment options for the disease. But, during that time, researchers were tirelessly working to better understand the genetic drivers of AML and testing potential treatments.

AML is an extremely heterogeneous disease. A wide range of mutations are involved and different drivers are responsible for the development of AML from patient to patient, and even cell to cell.³⁴ Preclinical models struggle to capture the heterogeneity of the disease making success in clinical trials less likely.³⁵ In the years since 1998, 91 medicines intended for AML failed in the development process having been discontinued, suspended, or had no development reported.³⁰ Meanwhile, 7 medicines received approval. That is a 13:1 ratio of unsuccessful attempts to FDA-approved medicines, but these setbacks laid the groundwork for the recent approvals as well as future progress. Outside of these setbacks, researchers are working to better understand how best to use these new treatments in combination or in a particular sequence.³⁶

Understanding which patients will benefit most from which approach is also an important area to expand our knowledge. In 2018, an extensive dataset for AML covering genomic, clinical, and drug data was published by a partnership called Beat AML. The partnership brought together 11 pharmaceutical and biotechnology companies as well as 11 academic medical centers. Over 30,000 data points were collected spanning across treatments and outcomes, pathology and genetic reports, demographics of patients, and diagnostic information. This data set has the potential to provide predictions for markers of drug sensitivity and resistance, in turn supporting the development of more effective drugs.³⁷

Finally, immunotherapy is a promising approach that has actually been used for AML for many years. Stem cell transplants are a form of immunotherapy and have been used for nearly four decades to treat AML. Researchers are currently working to better understand how AML interacts with the immune system and have identified multiple immune checkpoints that are involved including PD-1 and OX40. Clinical trials are currently underway targeting these pathways with checkpoint inhibitors. While PD-1 Inhibitors have been successful in several other forms of cancer, inhibitors of OX40 represent a novel approach.³⁸

Antibiotic Resistance and Cancer

Antibiotics play an important role in public health and are widely used in modern medicine in a variety of scenarios to fight off dangerous bacteria and avoid potentially life-threatening complications. But bacteria are becoming increasingly resistant to available antibiotics. According to the Centers for Disease Control and Prevention (CDC), antibiotic resistance is one of the biggest public health challenges of our time. Each year in the U.S., at least 2.8 million people get an antibiotic-resistant infection, and more than 35,000 people die.³⁹

For cancer patients undergoing treatment—resulting in weakened immune systems—effective antibiotics are critical. Cancer patients are at a higher risk of contracting serious infectious diseases and rely on antibiotics for the prevention and treatment of infections, which is one of the most common life-threatening complications of their illness and treatment. A recent survey found that 95% of the oncologists surveyed worry that antibiotic resistant bacteria will negatively impact the viability of chemotherapy.⁴⁰

Solutions for Advancing Value in Cancer Care⁴¹

Advances in regulatory science are creating efficiencies and enhancing the tools needed to drive innovative cancer drug discovery, development and approval. Solutions for accelerating cancer treatment progress include:

- Integrating the patient perspective by incorporating patient input and increasing patient engagement.
- Accelerating the qualification and use of biomarkers and increasing the acceptance of novel outcome measures and the development of tissue agnostic therapies.
- Advancing the use of real-world evidence by allowing the use of both safety and efficacy data in regulatory decision making.
- Increasing the acceptance of novel clinical trial design to enhance the use of adaptive and other flexible study designs.

Biopharmaceutical research companies are advancing patient-centered solutions for better value treatments and improving the use of medicines. Specifically, biopharmaceutical research companies are supporting the following principles:

- Expanding innovative contract uptake by advocating for modernization of outdated regulations.
- Leveraging new data, including real world data, and innovative tools to support informed decision-making by patients, physicians and payers on value.
- Developing quality measures that close gaps in clinical and patient-focused quality measures.

Sources:

1. American Cancer Society, Cancer Facts and Figures 2020; note: cancer survivorship as of 1/2019.
2. American Cancer Society, "Facts & Figures 2020 Reports Largest On-Year Drop in Cancer Mortality," January 8, 2020
3. S. Seabury, "Quantifying Gains in the War on Cancer Due to Improved Treatment and Earlier Detection," Forum for Health Economics and Policy 2016; 19(1): 141–156.
4. DN Lakdawala, et al., "An economic evaluation of the war on cancer," Journal of Health Economics. May 2010. 29(3):333-346.
5. Deaths: Final Data for 2017, National Center for Health Statistics
6. Global Cancer Observatory: Cancer Tomorrow. Lyon, France: International Agency for Research on Cancer. gco.iarc.fr/tomorrow.
7. American Association for Cancer Research. AACR Cancer Progress Report, Cancer in 2019.
8. Number of medicines obtained through public government and industry sources, and the Springer "AdisInsight" database; current as of December 4, 2020.
9. Johns Hopkins Medicine, www.hopkinsmedicine.org/health/conditions-and-diseases/gliomas#
10. www.ncbi.nlm.nih.gov/pmc/articles/PMC4322160/
11. Keytruda Label. www.accessdata.fda.gov/drugsatfda_docs/label/2020/125514s085lbl.pdf
12. Yervoy Label. www.accessdata.fda.gov/drugsatfda_docs/label/2018/125377s094lbl.pdf
13. In a First, FDA Approves Immunotherapy Combination for Advanced Melanoma, Cancer Research Institute, 1 October 2015
14. www.gene.com/media/press-releases/14868/2020-07-30/fda-approves-genentechs-tecentriq-plus-c
15. ASCO, PD-1 Inhibitor Pembrolizumab Provides Long-Term Survival Benefit for Patients with Advanced Melanoma, ascopost.com/News/40570
16. www.roche.com/media/releases/med-cor-2019-02-28.htm
17. www.roche.com/media/releases/med-cor-2020-06-29c.htm
18. Patentability standards for follow on pharmaceutical innovation. Jun 2018. Biotechnology Law Report.
19. The American Association of Pharmaceutical Scientists Journal. "Development of Fixed Dose Combination Products." Jun 6, 2019. www.ncbi.nlm.nih.gov/pubmed/31172358
20. www.prnewswire.com/news-releases/amgen-announces-launch-of-new-neulasta-pegfilgrastim-delivery-kit-300043818.html
21. Murthy VH, Krumholz HM, Gross CP: Participation in cancer clinical trials: race-, sex-, and age-based disparities. JAMA. 291:2720-6,2004.
22. Duma N, Vera Aguilera J, Paludo J, et al: Representation of Minorities and Women in Oncology Clinical Trials: Review of the Past 14 Years. J Oncol Pract. 14:e1-e10,2018.
23. Proportion of Study Volunteers by Race and Ethnicity in Clinical Research Studies, 2012. JNCI: Journal of the National Cancer Institute. 109, 2017.
24. Propublica. "Black Patients Miss Out on Promising Cancer Drugs" Published September 19, 2018, accessed June 23, 2019 at <https://www.propublica.org/article/black-patients-miss-out-on-promising-cancer-drugs>.
25. Unger JM, Gralow JR, Albain KS, et al: Patient Income Level and Cancer Clinical Trial Participation: A Prospective Survey Study. JAMA Oncol. 2:137-9, 2016.

26. [phrma.org/Codes-and-guidelines/PhRMA-Principles-on-Conduct-of-Clinical-Trials](https://www.phrma.org/Codes-and-guidelines/PhRMA-Principles-on-Conduct-of-Clinical-Trials)
27. catalyst.phrma.org/clinical-trials-q-and-a-income-disparities
28. Long, G. "The Biopharmaceutical Pipeline: Innovative Therapies in Clinical Development" Analysis Group. June 2017.
29. IMS Institute for Healthcare Informatics, "Innovation in Cancer Care and Implications for Health Systems: Global Oncology Trend Report," May 2014.
30. Researching Cancer Medicines – Setbacks and Stepping Stones, 2020, PhRMA
31. Parker Institute for Cancer Immunotherapy. "Brain Cancer Breakthrough with Immunotherapy Points to New Hope for Patients." <https://www.parkerici.org/the-latest/brain-cancer-breakthrough-with-immunotherapy-points-to-new-hope-for-patients/>
32. Science Daily, "New Glioblastoma Vaccine Shows Promising Results in Phase Ib Clinical Trial," 31 March 2019, www.sciencedaily.com/releases/2019/03/190331192548.htm
33. The benefits of immunotherapy combinations," 20 December 2017, www.nature.com/articles/d41586-017-08702-7
34. NJ Short, "Advances in the Treatment of Acute Myeloid Leukemia: New Drugs and New Challenges," Cancer Discovery, 3 February 2020, www.cancerdiscovery.aacrjournals.org/content/early/2020/02/02/2159-8290.CD-19-1011
35. E Estey, et al., "Current Challenges in Clinical Development of "Targeted Therapies": The Case of Acute Myeloid Leukemia," Blood, 2015, ashpublications.org/blood/article/125/16/2461/33755/Current-challenges-in-clinical-development-of
36. C Lai, et al. "Recent Drug Approvals for Acute Myeloid Leukemia." Journal of Hematology & Oncology, 2019; 100(12). jhoonline.biomedcentral.com/articles/10.1186/s13045-019-0774-x
37. National Cancer Institute. "Beat AML 1.0: A Collaborative Program for Functional Genomic Data Integration." www.cancer.gov/about-ci/organization/ccg/blog/2019/beataml
38. N Daver, "Immunotherapy Approaches in AML," Cancer Network, 17 January 2019, www.cancernetwork.com/acute-myeloid-leukemia/immunotherapy-approaches-aml
39. Centers for Disease Control and Prevention (CDC), www.cdc.gov/drugresistance/index.html
40. Pew Trusts. www.pewtrusts.org/en/research-and-analysis/articles/2020/03/11/oncologists-fear-rising-antibiotic-resistance-will-make-cancer-treatments-less-effective
41. Cancer Medicines: Value in Context, May 2019, PhRMA

