Promoting Value, Affordability, and Innovation in Cancer Drug Treatment

A Report to the President of the United States from the President's Cancer Panel

THE PRESIDENT'S CANCER PANEL

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This report is submitted to the President of the United States in fulfillment of the obligations of the President's Cancer Panel to appraise the National Cancer Program as established in accordance with the National Cancer Act of 1971 (P.L. 92-218), the Health Research Extension Act of 1987 (P.L. 99-158), the National Institutes of Health Revitalization Act of 1993 (P.L. 103-43), and Title V, Part A, Public Health Service Act (42 U.S.C. 281 *et seq.*).

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The President
The White House
Washington, DC 20500

Dear Mr. President,

The President's Cancer Panel concluded that addressing the dramatic rise of cancer drug prices must be made a national priority. Doing so will require a concerted, immediate, bipartisan, and multilateral effort. This report proposes balanced solutions aimed at growing a robust pipeline of innovative cancer drugs and ensuring that they are accessible to and affordable for those who need them.

The challenge at hand is complex. Innovative drugs offer new hope for patients to achieve long-term remissions—even cures—but virtually all new cancer drugs enter the market with a price tag that exceeds $100,000 per year and, increasingly, much higher. More and more patients are taking these novel drugs for months or even years. In addition, drug costs are accelerating far faster than costs for other components of care, which, together, can result in a significant financial burden on patients and their families. When financial resources are strained, patients are less likely to follow treatment regimens, potentially worsening health outcomes these drugs are intended to improve.

In this new era, there is an urgent need to ensure that drug prices are aligned with value. While high prices may be warranted for drugs that significantly extend survival and/or substantially improve quality of life, higher prices are not appropriate for drugs that do little to improve outcomes.

In developing this report, the Panel joined an ever-growing chorus of thought leaders and organizations calling for solutions to the problem of escalating drug prices. The Panel convened workshops in 2016-2017 with broad representation to ensure that the voices of many stakeholders and their respective viewpoints were heard. This included representatives of the pharmaceutical industry, healthcare providers, payers, and patients and their advocacy organizations, among others. Although the needs of all stakeholders are relevant when assessing the value of drugs, patients' benefit must be the central focus. In workshops, patients expressed appreciation for the drugs that have helped them live but also shock at the price tags. We heard patients say that their peers worry about having to choose between paying for their medicines or their mortgages. That is a choice no one in this country should have to make.

Stakeholders in every sector must work together to maximize value and affordability in cancer drug treatment and support investment in science that drives future innovation. The time to act is now. Mr. President, we urge you to support policies that propose sustained, predictable funding for government agencies that are working hard to provide the American people affordable access to innovative cancer drugs. We offer concrete actions that you can take in collaboration with public and private stakeholders identified in this report. You have the power to help minimize the financial toxicity experienced by many cancer patients and their families. Failure to act will delay the inevitable and create unfathomable burden for far too many Americans, even denying many the potential life-lengthening and life-saving benefits of a remarkable new generation of cancer drugs.

We share patients' optimism that innovation will result in more effective drugs—even cures—for cancer in the coming years and decades. We are pleased to share this report and our recommendations as a catalyst for action at this critical time. All cancer patients—now and in the future—should have affordable access to high-value drugs. For them, it is a matter of life and death.

Sincerely,

Barbara K. Rimer, DrPH

Hill Harper, JD

Owen N. Witte, MD

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EXECUTIVE SUMMARY

Innovations in cancer therapy, particularly the development of targeted drugs and immunotherapies, hold remarkable potential to transform treatment of the disease. Increasingly, a new generation of cancer drugs is producing durable remissions and, potentially, cures. However, prices for these drugs have risen dramatically in recent years. The United States faces the challenge and tension of creating both a robust pipeline of innovative cancer drugs while ensuring that these drugs are accessible and affordable for those who need them. For its 2016–2017 series of workshops, the President's Cancer Panel examined the drivers and impact of rising cancer drug prices in the United States and developed recommendations to address this problem.

The Panel concluded that urgent action is needed to address the ongoing, rapid increases in cancer drug costs—the health and lives of patients are at stake. This challenge can only be met through the input and action of all stakeholders—drug developers and manufacturers, policy makers, government, public and private payers, healthcare institutions and systems, providers, and patients.

Actions to address drug costs should follow several key guiding principles—**cancer drug prices should be aligned with their value to patients, all patients should have affordable access to appropriate cancer drugs, and investments in science are essential to drive future innovation**. Collectively, these actions will help us reach the ultimate goal of ensuring that all patients receive the treatment they need and experience the benefits that these remarkable drugs can offer.

PART 1: THE RISING COST OF CANCER DRUGS: IMPACT ON PATIENTS AND SOCIETY

The recent, dramatic rise in drug prices is straining patient, health system, and societal resources. Drugs account for about 20 percent of the total costs of cancer care in the United States, but cancer drug costs are accelerating faster than costs for other components of care. Launch prices of cancer drugs in the United States have risen so steeply over the past few decades that they have quickly outpaced growth in household incomes. U.S. patients and their insurers are paying more than ever for cancer drugs—$54,100 for a year of life in 1995 compared with $207,000 in 2013. Unfortunately, there are no signs that this price escalation is slowing.

The burden of high drug costs on patients—even those with health insurance—can be significant. Out-of-pocket spending on drugs can be hundreds, or even thousands, of dollars a month for patients in active treatment. Patients with higher out-of-pocket expenses are less likely to adhere to recommended treatment regimens, which may have a detrimental impact on outcomes. Although out-of-pocket expenses for drugs can be high, they are only one of many costs cancer patients face. The term **financial toxicity** describes the negative impact of cancer care costs on patients' well-being. Like medical toxicities caused by cancer treatment, financial toxicity can impose a significant burden on patients, including a diminished quality of life, interference with high-quality care delivery, and even a reduction in survival rates.

PART 2: TAKING ACTION TO PROMOTE VALUE, AFFORDABILITY, AND INNOVATION IN CANCER DRUG TREATMENT

Some cancer drugs have been transformative—significantly improving patients' outcomes and, in some cases, producing long-term remissions. However, many new drugs do not provide benefits commensurate with their prices. The Panel concluded that misalignment of drug prices and value is a critical problem that must be addressed. High-value drugs that cure cancer, significantly extend survival, and/or substantially improve quality of life should be priced higher than drugs that provide only modest benefits. They must be priced, however, within reach of the patients who need them. In this report, the Panel makes several recommendations to maximize value and affordability while continuing to support a pipeline of biopharmaceutical innovation. The ultimate goal is to ensure that all cancer patients—now and in the future—have affordable access to high-value drugs without experiencing financial toxicity.

While the focus of this report is on cancer drug costs and access, the Panel recognizes that rising cancer care costs overall also are a serious concern. Efforts to address cancer drug costs should be undertaken with consideration of the total cost of cancer care.

Recommendation 1. Promote value-based pricing and use of cancer drugs.

Steps must be taken to better align drug prices and costs with their value and promote use of high-value drugs. Achieving these goals could improve the quality of cancer care; create incentives for development of innovative, effective new drugs; and help address increases in drug spending that are threatening to put high-value drugs out of reach for some patients.

A Value Framework Is Needed to Facilitate Value-Based Pricing

There is no broadly accepted framework in the United States for determining whether cancer drug prices are aligned with their value. Defining the value of cancer drugs is challenging. Numerous factors influence value, and the relative importance of each of these factors depends on the perspective of the stakeholders—patients, providers, payers, healthcare systems, manufacturers, researchers, and society. Despite these challenges, cost can no longer be ignored if the United States aims to balance a robust innovation pipeline with treatment that is accessible and affordable for all cancer patients.

Developing and implementing a widely accepted value framework for cancer drugs is a critical step toward value-based pricing. Taking this step will require input and collaboration from all involved stakeholders, understanding that patient benefit must be central when assessing value. An ideal framework would integrate information on clinical outcomes, toxicities, impact on quality of life, and costs. It would inform negotiations between drug manufacturers and payers and also could guide development of value-based payment models and benefit designs that promote selection of high-value drugs by physicians and patients. Value assessments also could inform shared decision making among patients and providers and potentially improve patient outcomes.

Outcomes-Based Pricing for Cancer Drugs Should Be Explored

Outcomes-based risk-sharing agreements link payment for a drug to patients' outcomes. Under these agreements between payers and manufacturers, manufacturers are not paid or are paid less when patients do not achieve established clinical and/or quality-of-life outcomes. Although linking price to outcome does not guarantee value-based prices,

outcomes-based pricing has potential to improve alignment of drug price and value. More research is needed to determine the impact of outcomes-based pricing on value, quality, and costs for patients, providers, and payers, as well as the most effective and efficient ways to structure these agreements in various situations. Public and private payers and manufacturers should develop and pilot-test outcomes-based risk-sharing agreements for cancer drugs.

Payment Models Should Incentivize Providers to Use High-Value Drugs

The ways in which providers and healthcare organizations are paid influence choices about healthcare and how care is delivered. Under the prevailing fee-for-service payment model in the United States, providers are reimbursed largely based on the individual services and products they deliver. Current payment policies may create incentives for providers to deliver more services, prescribe more drugs, and/or prescribe higher-priced drugs. Physicians and hospital systems should be incentivized to recommend the highest-value treatment based on patients' clinical presentation and preferences, free of financial incentives to use higher-priced options. Ongoing healthcare reform efforts in the United States include alternative payment models that reward providers for providing high-quality, cost-efficient care rather than reimbursing them based solely on the volume of services delivered. Public and private payers should develop and test alternative payment models that support delivery of high-quality cancer care, including high-value drugs.

Insurance Plans Should Promote Patients' Use of High-Value Drugs

As drug costs have increased in recent years, many insurance plans have established drug tiers with different cost-sharing structures (patient out-of-pocket requirements) to steer beneficiaries toward preferred drugs. Value-based insurance design (VBID) offers a more patient-centered approach to insurance benefit design by aligning patients' out-of-pocket costs with the *value*—not the costs—of drugs and services. VBID may be well suited to cancer care due to the increasing role of high-cost specialty drugs and the growing capability to use biomarkers to match drugs with patients most likely to benefit. Public and private payers should develop and test VBID programs that promote patients' use of high-value cancer drugs.

Recommendation 2. Enable meaningful communication about treatment options, including cost information, to support patients' decision making.

After discussion with their cancer care teams, patients should be empowered to select treatments aligned with their needs, values, and preferences. To accomplish this, they must have accurate information about their disease, clear understanding of treatment options, and access to information about costs of treatment options. Cancer care teams should tailor this information to the needs, preferences, and comprehension capacity of individual patients.

Cancer patients express interest in communicating with their healthcare providers about cost, though such discussions are infrequent—only 27 percent of cancer patients and less than half of oncologists surveyed reported having had cost-related discussions. Research is needed to identify the best ways to communicate about cost and help patients include cost in their assessments of treatment value. It will be important to determine how cost discussions affect clinical decision making and clinical outcomes, as well as patients' quality-of-life, well-being, satisfaction, and financial toxicity.

Lack of transparency often makes it difficult for patients to know how much they will be charged for their care and the portion they will be responsible to pay out of pocket. The Panel urges payers and health systems to make cost and price information more widely available to patients and cancer care teams to facilitate informed decision making.

To enable value assessment of treatment options, cost information should be considered in conjunction with potential clinical benefits and harms, including impact on patients' quality of life. However, these data often are limited or unavailable. Physicians should clearly explain any evidence gaps to patients and should also tell patients when a drug is unlikely to provide benefit. In addition, health information technology should be leveraged to address these knowledge gaps.

Recommendation 3. Minimize the contributions of drug costs to financial toxicity for cancer patients and their families.

Patients' out-of-pocket costs for cancer drugs vary widely depending on a number of factors, such as cancer type, treatment plan, treatment setting, insurance status, and benefit design. High out-of-pocket drug expenses can have a detrimental impact on patients' care and well-being. Patients may decide not to fill their prescriptions, skip doses, or take less drug than prescribed to save money. Other patients may deplete their savings, incur debt, or forego spending on necessities to pay for their drugs. Steps should be taken to minimize the contributions of drug costs to financial toxicity for cancer patients and their families.

Health insurance—including prescription drug coverage—is a key factor in ensuring that drugs are affordable for cancer patients. As health insurance access has expanded, fewer Americans—including those with a history of cancer—report foregoing needed drugs because of cost. Future health policies should support and expand, not undermine, this progress. All Americans should have the opportunity to purchase reasonably priced, high-quality health insurance with prescription drug coverage to facilitate affordable access to cancer drugs.

As drug prices have increased, payers have shifted costs to patients through various cost-sharing mechanisms. Cost-sharing is an appropriate way to encourage judicious use of healthcare services, but it should not interfere with access to appropriate treatment or cause significant financial hardship. To protect people from excessive out-of-pocket costs, all public and private insurance plans should include out-of-pocket spending limits.

Recommendation 4. Stimulate and maintain competition in the generic and biosimilar cancer drug markets.

The United States incentivizes innovation, in part by granting patents and a number of exclusivities to manufacturers of new drugs and biologics. Once exclusivity ends, generic drugs and biosimilars can be approved, creating potential for competition and possibly driving down prices. Efforts must be made to facilitate timely and efficient market entry of generic and biosimilar drugs for cancer to bolster competition and ensure affordable access for patients.

The generic drug market has provided patients with affordable access to many drugs. In some cases, however, market forces or anticompetitive behaviors limit competition, which can lead to higher prices and/or drug shortages. The U.S. Food and Drug Administration (FDA) should reduce barriers for generic manufacturers to enter markets with no generic options or too few generic options to create competition. In addition, U.S. regulatory agencies and policy makers should continue to monitor and evaluate the generic drug market to identify factors that prevent healthy competition. Deliberate efforts to limit competition must be addressed. FDA also should continue to monitor the emerging U.S. biosimilars landscape and ensure that approval processes and manufacturing oversight are functioning efficiently such that biosimilar products can be made available to the American public.

Recommendation 5. Ensure that the FDA has appropriate resources to assess cancer drug safety and efficacy efficiently.

FDA plays a critical role in ensuring patient access to innovative cancer drugs. Cancer drug development

and evaluation present distinct challenges, particularly in the age of precision medicine. FDA has implemented policies and programs to address many of these challenges, and the Oncology Center of Excellence was established to enable more efficient and effective review of cancer treatments. The Panel supports the efforts of the Center.

An adequately staffed and well-resourced FDA is more important than ever in the modern era of oncology product development. A highly skilled FDA workforce also is essential as the agency considers important questions about incorporation of new kinds of data, including real-world evidence, into its review processes. The Panel urges the President and Congress to ensure that FDA has the resources and authority to assess the safety and efficacy of oncology products and to appropriately staff the Oncology Center of Excellence.

Recommendation 6. Invest in biomedical research to create a strong foundation for developing innovative, high-value cancer drugs.

A strong research infrastructure and workforce are essential to develop and deploy innovative, high-value drugs that potentially cure or, if not cure, significantly extend and improve the lives of cancer patients. The United States has long been a leader in biomedical research and pharmaceutical innovation, in large part because of cross-sector investment by government, industry, and nonprofit organizations. A vibrant discovery ecosystem is essential to ensure that the cancer drug pipeline continues to produce high-value products that benefit all patients.

The National Institutes of Health (NIH) is the world's leading funding organization for biomedical research. The work carried out by NIH-supported investigators has helped elucidate the molecular underpinnings of several cancer types and contributed to development of novel therapies. NIH training grants and career development programs play a critical role in building the U.S. biomedical research workforce. The Panel urges the President and Congress to provide sustained, predictable funding for NIH that, at a minimum, keeps pace with inflation. Failure to invest in NIH will threaten the United States' role as a global leader in the biomedical sciences and future progress against cancer. The Panel also urges continued commitment to cancer research by other sectors, including nonprofit and philanthropic organizations, venture capital companies, and the biopharmaceutical industry.

PART 3: CONCLUSIONS

Rising cancer drug costs are a significant problem and cannot be ignored—the consequences for patients, families, and society are too great. More than ever, affordable access to drugs will be the difference between life and death for cancer patients. The following principles should guide action:

- Cancer drug prices should be aligned with value to patients.
- All patients should have affordable access to appropriate cancer drugs.
- Investments in science are essential to drive future innovation.

This complex problem will not be solved quickly or easily, and it will not be solved by any organization or sector working alone. The Panel urges all stakeholders—drug developers and manufacturers, policy makers, government, public and private payers, healthcare institutions and systems, providers, and patients—to work together to address rising costs and ensure that patients have access to innovative, high-value, and affordable cancer drugs. The ultimate goal is to ensure that patients receive high-quality cancer treatment and experience the best possible health outcomes without financial toxicity.

PREFACE

The President's Cancer Panel was established in 1971 by the National Cancer Act (P.L. 92-218) and is charged with monitoring the progress of the National Cancer Program—which includes all public and private activities focused on preventing, detecting, and treating cancers and on cancer survivorship—and identifying barriers to effective implementation. The Panel investigates topics of high importance to the National Cancer Program for which actionable recommendations can be made. Information is collected through workshops and additional research. Findings and recommendations are compiled in reports to the President of the United States.

For its 2016-2017 series of workshops, the Panel examined the drivers and impact of rising cancer drug prices in the United States. The Panel convened three workshops to gather information from many stakeholders in this area, including patients, patient advocates, academic researchers, oncologists, health economists, statisticians, and intellectual property specialists, as well as representatives from federal agencies, insurance companies, and the biopharmaceutical industry.

Cancer drug prices in the United States have risen dramatically in recent years. Most new cancer drugs cost more than $100,000 per patient per year,[1,2] and per-patient spending on cancer drugs has increased at a much higher rate than spending on other components of cancer care.[3] Some patients may face out-of-pocket costs of nearly $12,000 per year for one drug.[4] These trends have been driven largely by the emergence and increased use of molecularly targeted drugs and immunotherapies. Some of these drugs have dramatically improved outcomes for patients, and additional promising therapies are on the horizon. However, some cancer drugs do not provide value commensurate with their prices. Drug prices have become an area of significant concern. A nationally representative survey found that more than 90 percent of Americans say cancer drugs are too expensive,[5] and high drug prices have garnered attention from the President,[6] Congress,[7,8] and medical professional organizations.[9,10] There is widespread agreement among these stakeholders that rising drug prices are a burden on cancer patients and are straining health system and societal resources.

The Panel concluded that steps must be taken to ensure that drug prices are aligned with their value and to promote use of high-value drugs. Like the American Society of Clinical Oncology (ASCO)[9] and the National Academies of Sciences, Engineering, and Medicine (NASEM),[11] the Panel believes that actions to promote value should be patient-centered and facilitate patients' access to appropriate treatments. It also is critical to recognize the importance of and maintain support for continued innovation in drug development. In this report, the Panel presents several recommendations for achieving these goals. While this report is presented to the President, it also is for a larger group of stakeholders—both public and private—that comprise the National Cancer Program. All of these stakeholders must work together to achieve the common goal of delivering innovative, high-value drugs to cancer patients at affordable prices.

Part 1:

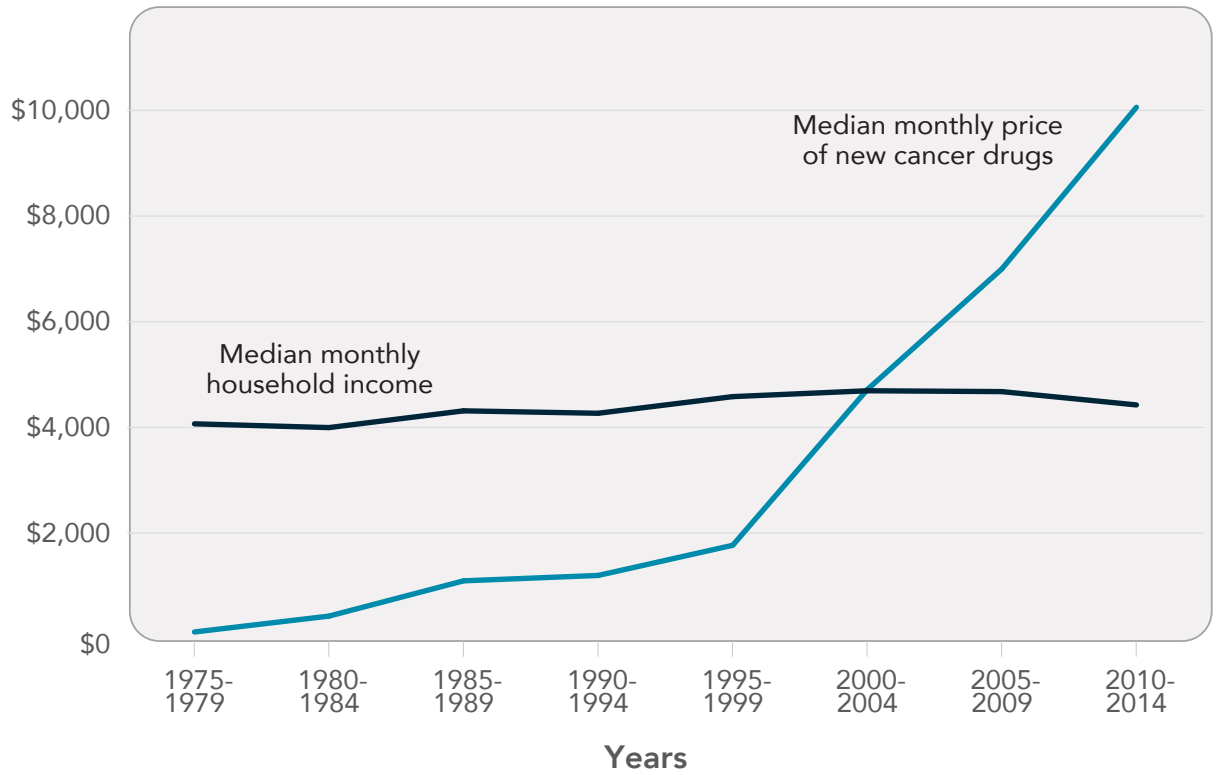
THE RISING COST OF CANCER DRUGS: IMPACT ON PATIENTS AND SOCIETY

Advances from basic science in understanding the molecular underpinnings of cancer and lessons from the clinical and population sciences are creating new opportunities to treat many cancer types effectively to produce extended remissions and, ultimately, cures. Biopharmaceutical companies are contributing to and capitalizing on this new knowledge. Several new therapies already have changed the cancer treatment landscape. The number of oncology drugs under development—also referred to as the oncology drug pipeline—grew by 63 percent between 2005 and 2015,[12] raising hopes that even more effective, potentially curative treatments are on the horizon. However, spending on cancer drugs has strained patient and societal resources and is a major cause for concern, particularly since the number of cancer cases is expected to rise as the U.S. population ages.[13] The United States faces the challenge and tension of creating both a robust pipeline of innovative cancer drugs while ensuring that these drugs are accessible and affordable for those who need them.

Cancer Drug Prices Are Increasing

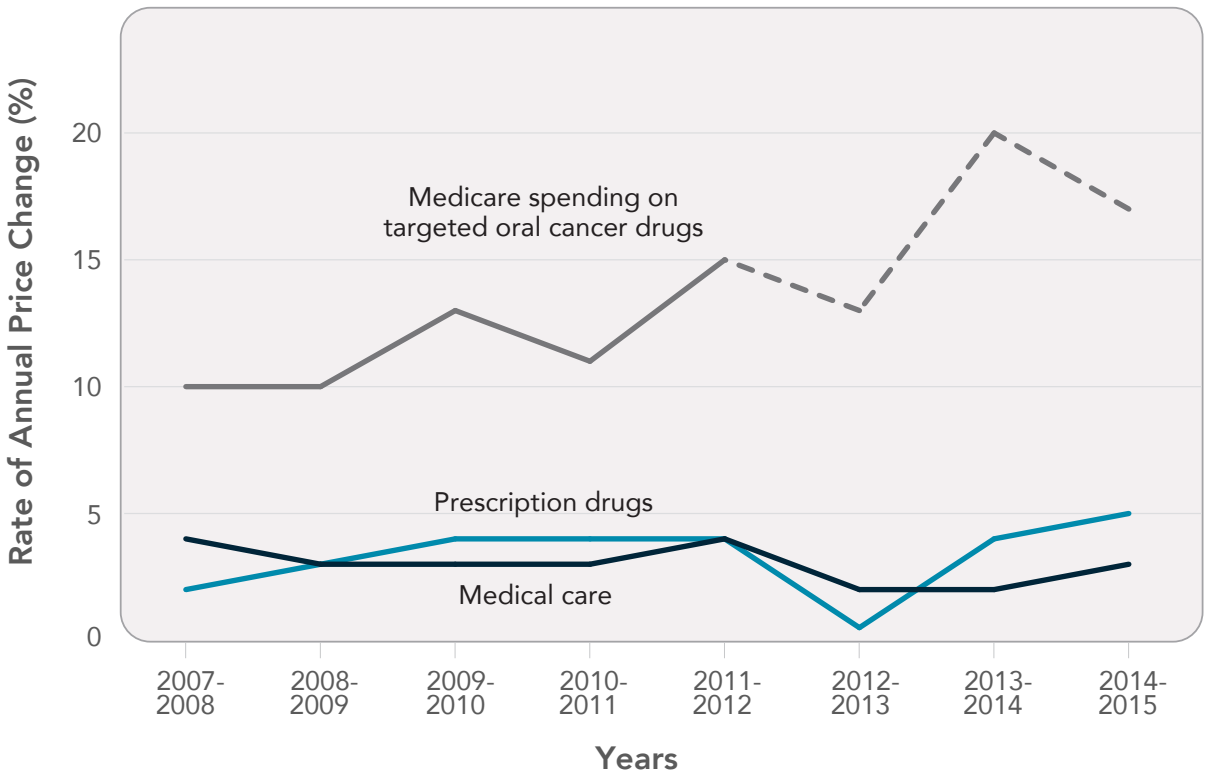
Remarkable scientific innovation has produced a growing number of immunotherapies and molecularly targeted therapies over the past couple of decades. Over the same time period, launch prices of cancer drugs in the United States have increased dramatically, vastly outpacing growth in household incomes since 1975 (Figure 1). There are no signs that this price escalation is slowing. Over half of new cancer drugs approved by the FDA between 2009 and 2013 were priced at more than $100,000 per patient for a year of treatment.[1] In 2015, new cancer drugs ranged in price from $7,484 to $21,834 per patient per month.[2]

Figure 1. Launch Price of New Cancer Drugs Compared with Household Income, 1975-2014



Source: Prasad V, Jesus K, Mailankody S. The high price of anticancer drugs: origins, implications, barriers, solutions. Nat Rev Clin Oncol. 2017.

Figure 2. Price Changes for Targeted Oral Cancer Drugs, Medical Care, and Prescription Drugs, 2007-2015



Note: Graph based on gross Medicare drug costs per patient per month. Dashed line represents projection on the basis of data published by the Centers for Medicare & Medicaid Services. Medical care and prescription drug data are based on Consumer Price Index data from the Bureau of Labor Statistics. **Source**: Shih YT, Xu Y, Liu L, Smieliauskas F. Rising prices of targeted oral anticancer medications and associated financial burden on Medicare beneficiaries. J Clin Oncol. 2017;35(22):2482-9. Reprinted with permission. © 2018 American Society of Clinical Oncology. All rights reserved.

Drugs account for about 20 percent of the total costs of cancer care, but cancer drug costs are accelerating faster than costs for other components of care. While total cancer care costs increased about 60 percent for commercially insured cancer patients between 2004 and 2014, spending on cytotoxic and biologic chemotherapies grew by 101 and 485 percent, respectively, over the same timeframe.[3] In addition, annual Medicare spending on targeted oral cancer drugs has increased dramatically, outpacing price increases for medical care and prescription drugs overall (Figure 2).[14] Increased spending is the result of higher drug prices, greater use of high-priced drugs, and an increase in the proportion of chemotherapy infusions being done in hospital outpatient settings, which is generally more expensive than administering drugs in physicians' offices.[3,15]

Some new cancer drugs have been transformative—significantly improving patients' outcomes and, in some cases, producing long-term remissions (see *Imatinib: Case Study of a Generic Cancer Drug* on page 22).[16] Innovative new therapies—such as chimeric antigen receptor T-cell (CAR-T) therapies[17,18]—also have potential to extend survival for many more patients. High prices may be warranted for drugs that significantly extend survival and/or substantially improve quality of life. Many new cancer drugs, however, do not provide clinically meaningful improvements as defined by ASCO.[19]

U.S. patients and their insurers are paying more than ever for cancer drugs—$54,100 for a year of life in 1995 compared with $207,000 in 2013[20]—but survival gains for most drugs still are measured in months.[19] Prices are similarly high for novel drugs and the "me-too" drugs that often follow,[1,21] and prices often increase substantially after launch.[22] Market entry of generic drugs has not reliably provided relief from high prices.[23-25] The emergence of combination therapies that include more than one high-priced drug will exacerbate the problem.[26]

The Toll of Drug Costs on Patients and Their Families

The burden of high drug costs on patients—even those with health insurance—can be significant. Out-of-pocket spending on drugs can be hundreds, or even thousands, of dollars a month for patients in active treatment.[4,14,15] Many patients are paying more for their drugs as insurance plans increasingly are charging coinsurance—a percentage of a drug's cost—rather than fixed copayments for prescription drugs.[27-30] As drugs extend survival, more patients are taking high-priced drugs for months, or even years, which may create long-term financial hardship. Patients with higher out-of-pocket expenses are less likely to adhere to recommended treatment regimens, which may have a detrimental impact on outcomes.[31-35]

Although out-of-pocket expenses for drugs can be high, they are only one of many costs cancer patients face. Costs of other components of care—surgery, radiation, hospitalization, and clinic visits—each often represent a higher share of treatment costs than drugs.[36,37] Many patients and their families and caregivers also experience indirect costs related to loss of income, and transportation and childcare costs, among other expenses.[38] Collectively, these costs can impose a significant burden on patients. Many cancer patients incur considerable debt as a result of their treatments[39] and/or reduce spending on basic necessities to defray out-of-pocket expenses.[40]

The term **financial toxicity** describes the negative impact of cancer care costs on patients' well-being (see *Financial Toxicity* on page 18). Like medical toxicities caused by cancer treatment, financial toxicity can significantly diminish patients' quality of life, interfere with high-quality care delivery, and even reduce survival rates.[41-45]

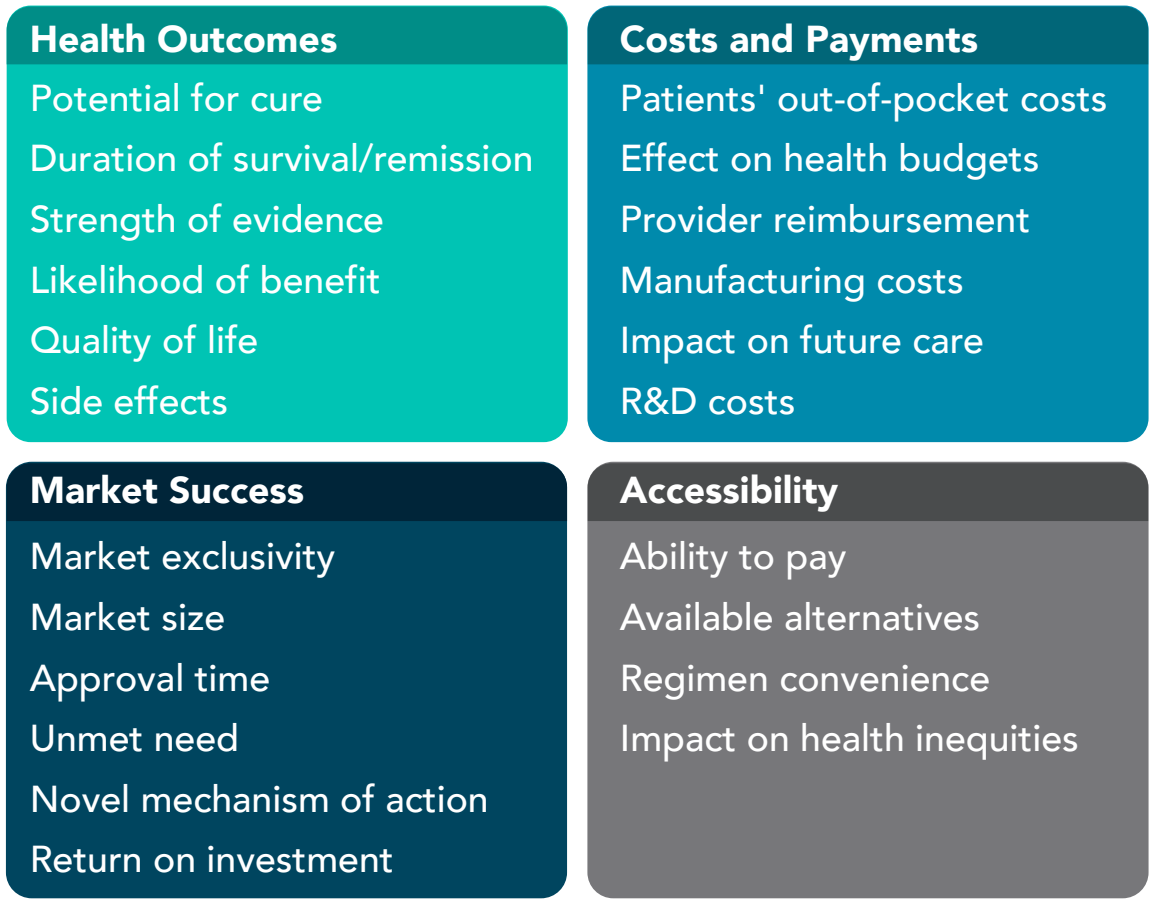
Action Is Needed to Ensure Patients' Access to High-Value Drugs

Drug development is an expensive and high-risk undertaking. While estimates vary widely, one recent study estimated the cost of developing a new drug at $2.6 billion,[46] and only 1 in 15 oncology drugs studied in Phase 1 clinical trials will make it to market.[47] Biopharmaceutical companies cannot be expected to incur the high costs of development without the potential for achieving financial benefits, including recovery of research and development costs, when drugs provide high value to patients. This is part of the cycle that drives future innovation. While drug developers should be rewarded financially for creating innovative drugs that provide high value to patients, it also is important that drugs are affordable and accessible for patients and society.

The President's Cancer Panel held a series of workshops in 2016-2017 to investigate the causes and consequences of rising cancer drug prices in the United States. During the series and in this report, drugs are defined broadly to include small molecules, biologics, and immunotherapies. **The Panel concluded that misalignment of drug prices and value is a critical problem that must be addressed. The costs of drugs should reflect the value to those who receive treatment—patients.** Defining the value of cancer drugs is challenging. Numerous factors influence value, and the relative importance of each of these factors depends on the perspective of the stakeholders—patients, providers, payers, healthcare systems, manufacturers, researchers, and society (Figure 3).[11] Though the needs of all stakeholders should be considered, patient benefit must be central when assessing value. In this report, the Panel makes

several recommendations to maximize value and affordability while continuing to support a pipeline of biopharmaceutical innovation. The ultimate goal is to ensure that all cancer patients—now and in the future—have affordable access to high-value drugs without experiencing financial toxicity.

Figure 3. Factors That Influence Cancer Drug Value



Stakeholders consider multiple factors when assessing the value of a cancer drug. The relative importance of these factors may vary among stakeholders, such as:

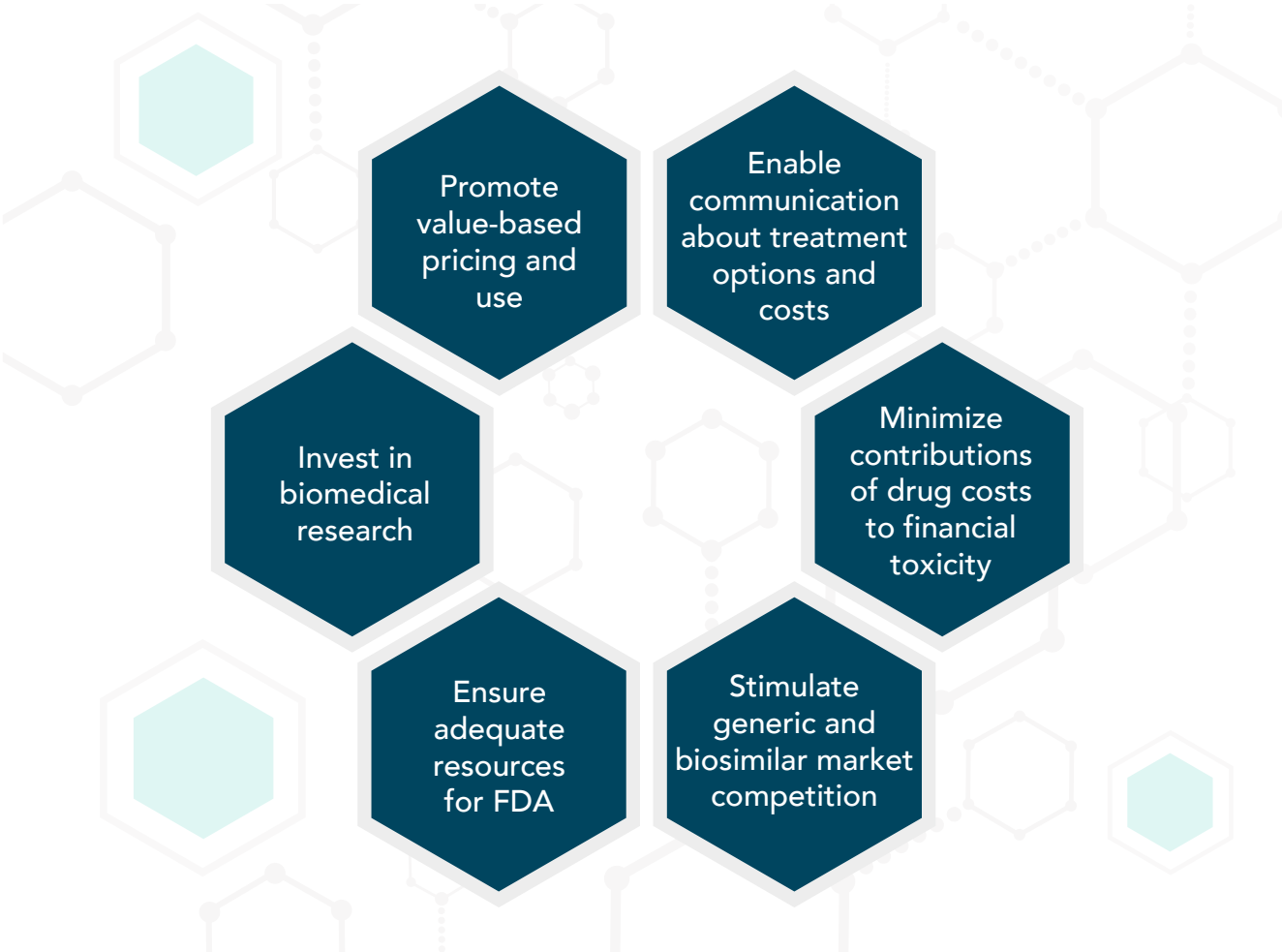
Patients | Providers | Healthcare Systems | Payers | Biopharmaceutical Companies | Researchers | Society

Part 2:

TAKING ACTION TO PROMOTE VALUE, AFFORDABILITY, AND INNOVATION IN CANCER DRUG TREATMENT

Cancer drug prices should be aligned with their value. High-value drugs that cure cancer, significantly extend survival, and/or substantially improve quality of life should be priced higher than drugs that provide only modest benefits. In addition to ensuring the best possible returns on healthcare spending, paying for cancer drugs based on value will incentivize future transformative innovation.[48] In this report, the President's Cancer Panel recommends several steps to promote value-based pricing and use of drugs, ensure patients' affordable access to high-value drugs, and promote future innovation (Figure 4). While the focus of this report is on drug costs and access, the Panel recognizes that rising cancer care costs overall also are a serious concern.[49] Efforts to address cancer drug costs should be undertaken with consideration of the total cost of cancer care.

Figure 4. President's Cancer Panel Recommendations



Recommendation 1

Promote value-based pricing and use of cancer drugs.

Drug prices have increased dramatically in the United States over the past several decades, particularly for cancer drugs (Figure 1).[50] A given drug has multiple prices and costs, including:

- List price set by the manufacturer;
- Negotiated prices paid by wholesalers, pharmacies, pharmacy benefit managers, insurance plans, hospitals, and healthcare practices; and
- Patients' out-of-pocket costs.

List prices for drugs are driven largely by what the market will bear, although manufacturers take into account a number of factors, including development costs, clinical efficacy, prices of other drugs on the market, and expected rebates.[1,51,52] Drugs pass through a series of "middlemen"—wholesalers, pharmacies, pharmacy benefit managers, hospitals, and healthcare practices— before reaching patients. Prices paid by these entities are determined through a complex and opaque system of negotiations, discounts, and rebates.[53] Patients' out-of-pocket costs depend on their insurance status and benefit plan structures. In some cases, these costs may be offset by patient assistance programs (see *Resources and Research Needed to Address Financial Toxicity* on page 20).

This complex process has resulted in drug prices that often do not reflect the benefits experienced by patients. **Steps must be taken to better align drug prices and costs with their value.** Achieving better alignment could improve the quality of cancer care; create incentives for development of innovative, effective new drugs; and help address increases in drug spending that are threatening to put high-value drugs out of reach for some patients.

A Value Framework Is Needed to Facilitate Value-Based Pricing

The Panel heard from many stakeholders that some form of value-based drug pricing should be adopted. However, there is no broadly accepted framework in the United States for determining whether cancer drug prices are aligned with their value. Defining the value of drugs is difficult, in part due to the different perspectives among stakeholders regarding the component of value (Figure 3). Despite these challenges, value frameworks that consider cost already are being used in several countries—including the United Kingdom, Canada, Australia, France, and Germany—to inform decisions about pricing, reimbursement, and government subsidization.[54] The United States, with its multiplicity of healthcare systems and payers, has been reluctant to incorporate cost and cost-effectiveness into value assessments, particularly in oncology.[55] Cost can no longer be ignored if the U.S. aims to balance a robust innovation pipeline with care that is accessible and affordable for all cancer patients. The Panel agrees with the NASEM that methods for determining the value of drugs should be tested and refined.[11]

Some efforts are under way—including those by the Institute for Clinical and Economic Review (ICER) and the Memorial Sloan Kettering Drug Pricing Lab[56] (see *Frameworks for Population-Level Assessment of Drug Value* on page 10)—to develop value frameworks for use in the United States, but none of these is yet widely accepted or used. Limitations noted for one or more of these frameworks include lack of patient-centeredness, lack of systemwide perspective, inadequate provisions for updates as new data are obtained, lack of transparency about methodologies, and failure to engage all stakeholders.[57-59]

Frameworks for Population-Level Assessment of Drug Value

The following population-level value assessment tools are being developed for use by payers, policy makers, and other system-level stakeholders. Tools to facilitate physician and patient consideration of value are discussed in Recommendation 2.

- The Institute for Clinical and Economic Review value assessment framework includes a conceptual framework and set of associated methods used to develop evidence reports. ICER reports cover several disease areas and are intended to support deliberation on medical policies related to health services—including, but not limited to, drugs—and delivery system interventions.

- Drug Abacus, a tool developed by the Memorial Sloan Kettering Drug Pricing Lab, is designed to calculate prices for cancer drugs based on efficacy, toxicity, novelty, research and development costs, unmet need, and other factors. Drug Abacus focuses on cancer drugs and has been used to evaluate 52 cancer drugs approved by the U.S. Food and Drug Administration between 2001 and 2015.

Developing and implementing a widely accepted value framework for cancer drugs is a critical step toward value-based pricing. An ideal framework would integrate information on clinical outcomes, toxicities, impact on quality of life, and costs. Multiple forms of evidence should be taken into account, including, but not limited to, patient-reported outcomes, results from randomized clinical trials, and real-world evidence (as appropriate). Such a framework would inform negotiations between drug manufacturers and payers and also could guide development of value-based payment models and benefit designs that promote selection of high-value drugs by physicians and patients, both of which are discussed later in this section.[60] Robust value assessments could help ensure that manufacturers are financially incentivized to produce drugs that provide substantial benefit to patients and enable payers to make informed decisions about coverage based on value. Value assessments also could inform shared decision making among patients and providers and potentially improve patient outcomes (Recommendation 2).

NASEM should convene a committee to review the strengths and limitations of value frameworks being developed and/or used in the United States and other countries and determine whether these frameworks could be used to assess cancer drug value in the United States. The committee should take into account the guiding principles for value frameworks identified by the Panel (see *Guiding Principles for Value Frameworks* on page 11) and others.[59,61-64] A range of stakeholders and experts should be included on the committee (see *Stakeholders and Experts* on page 11). Any identified opportunities to improve upon existing frameworks should be reported. If warranted, NASEM should develop a new framework for assessing the value of cancer drugs. In addition, the committee should recommend ways in which existing or new value frameworks should be tested and implemented. The U.S. healthcare and health insurance landscapes are distinct from those in other countries, which may have implications for value assessment processes and establishment of appropriate thresholds for value. Value thresholds should be high enough to encourage innovation in drug development.

Guiding Principles for Value Frameworks

- Include all stakeholders throughout framework development, testing, and implementation.
- Emphasize and measure factors that matter most to patients.
- Examine patient subgroups (e.g., molecularly defined) whenever possible and appropriate.
- Gather and synthesize evidence in a transparent manner using accepted practices.
- Use all high-quality evidence currently available (e.g., clinical trial results, real-world evidence, patient-reported outcomes).
- Acknowledge gaps in data and conflicting data when appropriate.
- Consider all healthcare costs and potential cost savings (e.g., for hospitalization, surgery), not only drug costs.
- Ensure that assessments of new drugs and updates based on new data are completed in a timely manner.
- Ensure that results can be readily interpreted and used.

Stakeholders and Experts

- Patients and patient advocates
- Physicians and other care team members
- Healthcare systems
- Public and private payers
- Pharmacy benefit managers
- Policy makers
- Biopharmaceutical and diagnostics companies
- Ethicists
- Researchers with relevant expertise, including health economists
- Developers and users of existing frameworks

Some policy makers and organizations have advocated changes to the Medicare Modernization Act (P.L. 108-173) that would allow the Secretary of the U.S. Department of Health and Human Services to negotiate drug prices for Medicare Part D, which currently is prohibited.[65] However, it is unclear whether the Secretary would be able to achieve significantly greater savings than currently negotiated by private Part D plan sponsors.[65,66] Negotiations between both public and private payers likely would be supported more effectively by developing a framework to assess drug value. The Panel also heard from several workshop participants that coverage mandates requiring Medicare and commercial insurance plans in many states to cover all FDA-approved cancer drugs undermine negotiation of value-based prices.[67-69] While this may be true, the Panel is concerned that eliminating current mandates may compromise patients' access to high-value cancer drugs if other safeguards are not in place. State and federal policy makers should continue to monitor the landscape of cancer drug pricing to determine whether changing circumstances warrant eliminating or modifying coverage mandates. Narrower mandates based on drugs' value may serve patients better than the current system.

Outcomes-Based Pricing for Cancer Drugs Should Be Explored

Outcomes-based risk-sharing agreements (sometimes called performance-based risk-sharing agreements) link payment for a drug to patients' outcomes.[70,71] Under these agreements between payers and manufacturers, manufacturers are not paid or are paid less when patients do not achieve established clinical and/or quality-of-life outcomes. Outcomes-based pricing for cancer drugs may be appealing for a few reasons:

- High-cost cancer drugs pose a financial risk for payers.
- Many cancer drugs receive accelerated FDA approval based on surrogate endpoints.
- Manufacturers may be interested in providing incentives for use of these drugs to expand the evidence base of their drug's efficacy in clinical settings.

To date, outcomes-based pricing has been used most widely in countries with single-payer healthcare systems (e.g., Europe, Canada, Australia).[70] However, interest in outcomes-based pricing has increased in the United States in recent years. A recent review of U.S. risk-sharing agreements since 1997 found that nearly two-thirds had been announced or initiated in or after 2015.[72] About 20 percent of these agreements involved cancer drugs. Interest in risk-sharing agreements is expected to increase with the growing availability and use of high-priced drugs and the mounting emphasis on accountable care.[73] The Centers for Medicare & Medicaid Services (CMS) recently announced it is working actively with stakeholders on innovative payment arrangements, which may include outcomes-based pricing for drugs.[74] Novartis announced it is collaborating with CMS to make outcomes-based pricing available for its recently approved novel cancer gene therapy, tisagenlecleucel.[70,75] Private payers also have expressed interest in outcomes-based pricing and are exploring ways to more closely align prices with patients' outcomes.[70,76]

Outcomes-based pricing has potential to improve alignment of drug price and value. It also may encourage manufacturers to invest in research to identify patient subgroups most likely to respond to their drugs, which could further increase value. However, linking price to outcomes does not guarantee value-based prices, even when patients respond to a drug. The price still may be higher than warranted for the level of benefit. It also does not ensure higher quality of care, lower overall costs for payers, or lower out-of-pocket costs for patients.[77,78] Payers and manufacturers must resolve several challenges when negotiating outcomes-based risk-sharing agreements, including defining meaningful outcomes and addressing lack of control over how a drug will be used by physicians and patients.[70]

More research is needed to determine the impact of outcomes-based pricing on value, quality, and costs for patients, providers, and payers, as well as the most effective and efficient ways to structure these agreements in various situations. For example, regulatory factors may vary depending on whether agreements involve public or private payers.[79] **Public and private payers and manufacturers should develop and pilot-test outcomes-based risk-sharing agreements for cancer drugs.** These agreements should be structured to ensure that patients' out-of-pocket costs also are tied to outcomes. Evaluations should be rigorous and transparent, and results should be disseminated consistently to inform future efforts.

Payment Models Should Incentivize Providers to Use High-Value Drugs

The ways in which providers and healthcare organizations are paid influence choices about healthcare and how care is delivered.[80] Under the prevailing fee-for-service payment model in the United States, providers are reimbursed largely based on the individual services and products they deliver. Current payment policies may create incentives for providers to deliver more services, prescribe more drugs, and/or prescribe higher-priced drugs.[20,81] For example, Medicare Part B reimburses for most covered drugs based on the average sales price plus a 6 percent add-on, which means that providers' revenue is higher for higher-priced drugs. The 340B Drug Pricing Program—which significantly increases the profit margins of certain drugs at participating hospitals—also creates financial incentives to prescribe more drugs or higher-priced drugs.[82]

Drug payment policies based on volume and price have garnered significant attention, but efforts by CMS and the Medicare Payment Advisory Commission to modify incentive structures have faced strong resistance from physician groups, drug manufacturers, and patients.[83,84] Opponents have argued that the ultimate goals of increasing quality, lowering costs, and improving patients' experiences will more likely be achieved by comprehensive oncology payment reform rather than through targeted reform of drug payment policies.[85] Physicians and hospital systems should be incentivized to recommend the highest-value treatment based on patients' clinical presentation and preferences, free of financial incentives to use higher-priced options. Implementation of drug payment reform faces many challenges, including the potential for targeted changes in drug payment policies to negatively impact other aspects of care. **As such, the Panel recommends that drug cost and value be considered and addressed within the larger context of cancer care payment reform.**

Ongoing healthcare reform efforts in the United States include alternative payment models (APMs) that reward providers for providing high-quality, cost-efficient care rather than reimbursing them based solely on the volume of services delivered. An oncology-specific APM—the Oncology Care Model—currently is being pilot tested (see *Oncology Care Model* on page 14).[86] ASCO[87] and the American Society for Radiation Oncology[88] also have developed oncology APMs. Private payers have been experimenting with new ways to pay for cancer care with the goal of promoting quality of care while reducing costs.[89]

Oncology Care Model

The Center for Medicare & Medicaid Innovation launched the Oncology Care Model (OCM) in 2016. This five-year physician specialty model aims to improve care coordination, appropriateness of care, and access to care for Medicare beneficiaries undergoing chemotherapy. A total of 190 oncology practices that provide care for an estimated 150,000 Medicare beneficiaries each year volunteered to participate in OCM. Participating practices receive:

- Regular fee-for-service Medicare payments;
- Additional monthly per-patient payments to support care coordination; and
- Performance-based payments if they achieve OCM quality measures and reduce expenditures below a target price.

Fourteen commercial payers have agreed to align cancer payment and quality measurement approaches with OCM, which should ease implementation for practices and hopefully deliver benefits to a broader patient population. The results of this pilot should inform future oncology payment reform efforts.

Aligning provider incentives with value is a laudable goal, but producing meaningful improvements in the complex and fragmented realm of U.S. healthcare will continue to be challenging. Changes should be informed by evidence, and unintended consequences should be identified and addressed. This requires careful and thorough evaluation of several payment models. **Public and private payers should develop and test alternative payment models that support delivery of high-quality cancer care, including high-value drugs.** Oncology-specific APMs should promote use of high-value cancer drugs and support future innovation by: [90,91]

- Providing incentives for evidence-based care (e.g., clinical pathways);
- Encouraging first-line use of the least-costly treatment option if two or more equally effective regimens are available;
- Allowing flexibility to appropriately tailor treatments to individual patients' needs and preferences;
- Incorporating mechanisms to enable rapid adoption of innovative drugs as evidence is generated; and
- Facilitating patients' participation in clinical trials.

APMs should take into account how a treatment regimen will impact other healthcare spending (e.g., hospitalization, surgery, other drugs). Consideration should be given to how payment models will be implemented in clinical settings. Programs should be adaptable to fit clinical workflows in multiple settings. Providers' and patients' experiences also should be taken into account when programs are being evaluated.

Insurance Plans Should Promote Patients' Use of High-Value Drugs

As drug costs have increased in recent years, many insurance plans have established drug tiers with different cost-sharing structures (patient out-of-pocket requirements) to steer beneficiaries toward preferred drugs. Most new cancer drugs are included in

specialty tiers with high cost-sharing requirements; many plans require patients to pay coinsurance of 25 to 50 percent of the drug's cost.[92,93] High cost-sharing can contribute to financial toxicity and, in some cases, cause patients to forego recommended or cease efficacious care.[31-35]

Value-based insurance design offers a more patient-centered approach to insurance benefit design by aligning patients' out-of-pocket costs with the *value* —not the costs—of drugs and services. For example, highly effective drugs, even high-priced ones, would be available to patients at low or no cost.

VBID programs implemented by private and public payers have led to some improvements in treatment adherence and lowered patient out-of-pocket spending for chronic diseases, such as asthma, diabetes, and hypertension.[94] However, the potential for VBID to improve adherence to and affordability of cancer drugs has not yet been evaluated. VBID may be well suited to cancer care due to the increasing role of high-cost specialty drugs and the growing capability to use biomarkers to match drugs with patients most likely to benefit.[95,96] **Public and private payers should develop and test VBID programs that promote patients' use of high-value cancer drugs.** In addition to reducing or removing financial barriers to high-cost specialty drugs when these treatments are the best option for cancer patients, payers should consider increasing out-of-pocket costs for low-value drugs and services. This strategy could increase quality of care and help cover the cost of VBID programs.[97,98] Policies and regulations should be modified as needed to enable testing and implementation of VBID programs.

VBID should be applied to both infused and oral chemotherapies. Dramatically different benefit designs for drugs based on mode of administration is not consistent with value-based pricing and incentives. Cost-sharing also should be structured fairly. The Panel is troubled by the fact that Medicare Part D beneficiaries pay coinsurance based on drug prices that do not take into account the rebates paid by manufacturers to pharmacy benefit managers, which often are substantial.[99] Medicare Part D and other insurance plans should calculate patients' coinsurance based on the expected net price for the drug after rebates. Benefit plans also should include out-of-pocket spending limits to help protect patients from financial toxicity (Recommendation 3).

Recommendation 2

Enable meaningful communication about treatment options, including cost information, to support patients' decision making.

After discussion with their cancer care teams, patients should be empowered to select treatments aligned with their needs, values, and preferences. To accomplish this, they must have:

- Accurate information about their diagnosis and prognosis;
- Clear understanding of recommended treatment options, including treatment purpose (e.g., cure, extended survival, palliation);
- Realistic expectations about possible clinical benefits and harms of treatment options; and
- Access to information about costs of treatment options.

Cancer care teams should tailor this information to the needs, preferences, and comprehension capacity of individual patients. This type of "precision communication" is essential to patient-centered cancer care.

Historically, discussions about cost have not been part of clinical care for cancer, but the Panel agrees with recommendations by the Institute of Medicine[100] and ASCO[101] that patients should be informed about the costs of care; in particular, out-of-pocket costs.

In one survey, more than one-third of cancer patients reported higher than expected out-of-pocket costs, which was associated with increased likelihood of financial distress.[102] Access to cost information potentially would enable patients to integrate costs, as they desire, into their personal value assessments of treatment options. Cost information also may help patients, families, and care teams identify ways to prevent or address financial toxicity (Recommendation 3).

Effective communication about drug value may lead to lower costs, but providing cost information to patients should not be viewed as a cost containment strategy. Cost should never hinder patients' access to appropriate cancer treatments (Recommendation 1 and Recommendation 3).

Discussions of Treatment Cost and Value Should Be Improved

Nearly two-thirds of cancer patients express interest in communicating about cost, and most oncologists agree that patients should understand the financial implications of their treatment options. Despite this, discussions about cost are infrequent—only 27 percent of cancer patients and less than half of oncologists surveyed reported having had cost-related discussions.[103]

Nearly 2/3 of cancer patients expressed interest in communicating about cost, but only 27% reported having had cost-related discussions with their physicians.

Research is needed to identify the best ways to communicate about cost and to help patients include cost in their assessments of treatment value. It will be important to determine how cost discussions affect clinical decision making and clinical outcomes, as well as patients' quality-of-life, well-being, satisfaction, and financial toxicity. Several groups—including ASCO[104] and the National Comprehensive Cancer Network[105] (see *Clinical Tools to Assess Treatment Value* below)—have begun developing tools to help physicians and patients incorporate cost into cancer treatment value assessments. The Patient-Perspective Value Framework developed by Avalere and FasterCures identifies additional patient and family costs that should be included in value assessments.[64] These tools should be formally evaluated to determine whether they result in improved communication and decision making. Tools and strategies must be optimized for easy integration into clinical workflows and tailored to the specific circumstances of individual patients. Moreover, such tools and discussions should be developed and calibrated in recognition of patients' diversity to ensure that cancer care disparities that disadvantage socioeconomically deprived patients are not created or exacerbated.

Clinical Tools to Assess Treatment Value

ASCO has developed a Value Framework that assesses cancer therapies based on clinical benefit, side effects, improvements in patient symptoms, and cost. One possible future step could be to create an electronic, physician-guided tool that can be modified at the point of care to reflect patient priorities and used to support shared decision making.

The National Comprehensive Cancer Network has developed Evidence Blocks to accompany its Clinical Practice Guidelines. The Evidence Blocks provide a visual representation of five key measures—efficacy, safety, quality of evidence, consistency of evidence, and affordability—with the goal of supporting informed decision making by providers and patients.

Patients Should Have Access to Cost Information

Lack of transparency often makes it difficult for patients to know how much they will be charged for their care and the portion they will be responsible to pay out of pocket.[106,107] These numbers may vary considerably depending on the healthcare facility and patients' insurance benefit plans. While there have been some efforts to address the problem—including price transparency laws in some states requiring health practices and hospitals to provide cost information and addition of cost-related features on insurance company websites—more extensive transparency is needed.[108] **The Panel urges payers and health systems to make cost and price information more widely available to patients and cancer care teams to facilitate informed decision making.** In addition, research is needed to determine what information is most useful to patients (Recommendation 3).

Clinical Data Are Needed to Inform Decision Making

To enable value assessment, cost information should be considered in conjunction with potential clinical benefits and harms, including impact on patients' quality of life. Ideally, each patient should be able to review clinical data that reflect outcomes in other patients with similar diseases and health characteristics. However, these data often are limited or unavailable, in part because clinical trial populations often are not representative of the general population. Moreover, a paucity of data exists on quality of life and patient-reported outcomes because they are collected inconsistently and in nonstandardized formats, if at all. Physicians should clearly explain any evidence gaps to patients and should also tell patients when a drug is unlikely to provide benefit.

As discussed in the Panel's 2016 report, *Improving Cancer-Related Outcomes with Connected Health*,[109] widespread adoption of health information technology is creating opportunities to address these knowledge gaps. In particular, standardized collection of patient-reported outcomes and use of learning healthcare systems that gather and analyze real-world data could generate valuable information for physicians and patients weighing treatment options. The need to "unleash the power of data" to improve cancer care and research also is a key theme in the 2016 *Report of the Cancer Moonshot Task Force*.[110]

Recommendation 3

Minimize the contributions of drug costs to financial toxicity for cancer patients and their families.

Patients' out-of-pocket costs for cancer drugs vary widely depending on a number of factors, such as cancer type, treatment plan, treatment setting, insurance status, and benefit design.[37,38] The shift toward high-priced specialty drugs—which include most targeted therapies and immunotherapies—has substantially increased out-of-pocket costs for many patients. For example, average out-of-pocket costs for cancer drugs increased from $450 per month in 2001 to $647 per month in 2011 for nonelderly, privately insured patients, coinciding with an increase in use of targeted cancer drugs.[15] These costs are likely to rise in the future with the advent of more immunologic therapies that have potential to be highly effective.

Although drugs are not the most expensive part of cancer care for most patients,[36,37] drug costs are a significant concern for patients and their families. A nationally representative survey found that more than 90 percent of Americans think the cost of cancer drugs is too high.[5] High out-of-pocket drug expenses can have a detrimental impact on patients' care and well-being. Several studies of different patient populations have found that those with higher out-of-pocket costs for drugs are less likely to adhere to their treatment regimens.[31-35] Patients may decide not to fill their prescriptions, skip doses, or take less drug than prescribed to save money.[5,34]

Financial Toxicity

The term **financial toxicity** describes the negative impact of cancer care costs on patients and their families and caregivers. Like medical toxicities caused by cancer treatments, financial toxicity can cause significant distress, influence decisions about treatment, affect adherence to treatment, and shorten survival. Caregivers also may face financial strain if they must take significant time off from work during treatment and recovery. Financial toxicity results from a confluence of many factors, including out-of-pocket spending for drugs and other healthcare, indirect costs of care (e.g., transportation, childcare), loss of income for patients and caregivers, and insufficient financial resources. Younger patients and those with lower household incomes are at higher risk of treatment-related financial hardship.

Sources: PDQ Adult Treatment Editorial Board. Financial toxicity and cancer treatment [Internet]. Bethesda (MD): National Cancer Institute; [updated 2016 Dec 14; cited 2017 Apr 13]. Available from: https://www.cancer.gov/about-cancer/managing-care/track-care-costs/financial-toxicity-hp-pdq; President's Cancer Panel. Living beyond cancer: finding a new balance. Bethesda (MD): the Panel; 2004 May. Available from: https://deainfo.nci.nih.gov/advisory/pcp/annualReports/pcp03-04rpt/Survivorship.pdf

Other patients may deplete their savings, incur debt, or forego spending on necessities to pay for their drugs.[111,112] Nonadherence to treatment regimens and experiencing significant financial hardship as a result of paying for care are examples of financial toxicity (see *Financial Toxicity* above and *Resources and Research Needed to Address Financial Toxicity* on page 20). **Steps should be taken to minimize the contributions of drug costs to financial toxicity for cancer patients and their families.**

High-Quality Health Insurance Facilitates Affordable Access to Cancer Drugs

Health insurance—including prescription drug coverage—is a key factor in ensuring that drugs are affordable for cancer patients. Insurance plans negotiate reduced prices for their beneficiaries and usually cover a portion of drug costs. Uninsured patients are responsible for the full cost of their care, potentially leading to much higher out-of-pocket expenses. For example, the estimated patient responsibility for an infusion of gemcitabine—a drug used to treat breast, lung, ovarian, and pancreatic cancers—was $50 for Medicare beneficiaries compared with more than $2,000 for uninsured patients.[113] Few patients can afford to pay these prices.

In 2017, over 90 percent of people in the United States had health insurance coverage, more than at any time in the past.[114] As health insurance access has expanded, fewer Americans—including those with a history of cancer—report foregoing needed drugs because of cost.[115] In addition to improved access to drugs,[116] patients with health insurance are more likely to receive recommended screenings, less likely to be diagnosed with late-stage cancer, and more likely to survive after diagnosis.[111,117] Future health policies should support and expand, not undermine, this progress. **All Americans should have the opportunity to purchase reasonably priced, high-quality health insurance with prescription drug coverage to facilitate affordable access to cancer drugs.** Limiting access to potentially lifesaving drugs could have devastating, possibly life-threatening consequences for cancer patients.

Patients' Out-of-Pocket Expenses Should Be Limited to Minimize Financial Toxicity Caused by Cancer Drug Costs

As drug prices have increased, payers have shifted costs to patients through various cost-sharing mechanisms. An increasing number of plans are charging coinsurance—which is a percentage of

a drug's cost—rather than fixed copayments for prescription drugs. Coinsurance rates have increased in recent years, and many cancer drugs—including some generics—are placed on specialty tiers with higher rates of coinsurance.[27-30] Drug prices also have contributed to insurance premium increases—about 14 percent of premium increases in 2017 were attributed to drugs.[118] Increased cost-sharing has led to higher rates of underinsurance—defined as high out-of-pocket costs relative to income—among people with health insurance.[119] Cost-sharing is an appropriate way to encourage judicious use of healthcare services (Recommendation 1), but it should not interfere with access to appropriate treatment or cause significant financial hardship. To protect people from excessive out-of-pocket costs, all public and private insurance plans should include out-of-pocket spending limits.

Many insurance plans already limit patients' out-of-pocket expenses. Since 2014, all commercial insurance plans have been subject to annual out-of-pocket spending limits under the Affordable Care Act. Costs contributing to out-of-pocket maximums include deductibles, coinsurance, copayments, and other similar charges.[120] For the 2018 plan year, out-of-pocket limits cannot exceed $7,350 for individuals and $14,700 for family plans (actual out-of-pocket limits vary by plan and are often lower than required).[121,122] Cost-sharing subsidies paid by the federal government reduce out-of-pocket limits for low- and moderate-income individuals and families who purchase plans through the health insurance exchanges.[123] Though out-of-pocket caps will not protect all patients from financial toxicity, they undoubtedly provide relief to many people facing cancer diagnosis and treatment.[124] **The Panel agrees with the American Cancer Society Cancer Action Network[125] that limits on out-of-pocket spending should be maintained to help protect cancer patients from financial toxicity caused by costs of drugs and other components of care.**

There are no out-of-pocket spending limits for most beneficiaries of Medicare Part D, Medicare's prescription drug benefit plan.* Part D covers most orally administered cancer drugs, which account for a rapidly growing proportion of cancer drug costs.[12] Unsubsidized Part D beneficiaries being treated with targeted oral cancer drugs paid an average of $810 per month out-of-pocket in 2012.[14] Although this is lower than patients' costs in earlier years (due to the closing of the coverage gap),† it may cause financial hardship for many patients.

Some patients may face out-of-pocket costs of nearly $12,000 per year for one drug.

A growing number of Part D beneficiaries are reaching the catastrophic threshold,[126]† in part because of the increased availability and use of high-priced drugs.[127] Once this threshold is reached, patients are required to pay 5 percent of the price of their drugs.[126] Costs can add up quickly, particularly for patients who must take specialty drugs for months or years. Some patients may face out-of-pocket costs of nearly $12,000 per year for one drug.[4] **The Panel agrees with NASEM and the Medicare Payment Advisory Commission that Medicare Part D should eliminate cost-sharing for patients above the catastrophic threshold.**[11,128] Out-of-pocket spending limits may result in higher premiums for all Medicare beneficiaries or increased cost-sharing before out-of-pocket limits are reached. However, this scenario is preferable to imposing unlimited costs on patients dealing with serious diseases like cancer.

* There are out-of-pocket spending limits for the approximately 30 percent of Part D beneficiaries who qualify for the Low-Income Subsidy.

† The coverage gap, sometimes called the doughnut hole, refers to the gap in Medicare Part D coverage after beneficiaries reach the initial coverage limit and before they reach the threshold for catastrophic coverage ($4,950 out-of-pocket spending for drugs under the standard benefit in 2017). When Medicare Part D was established in 2006, beneficiaries were responsible for the full cost of their drugs within the coverage gap (100% coinsurance). The Affordable Care Act included provisions to gradually reduce coinsurance rates to 25 percent between 2011 and 2020.

Resources and Research Needed to Address Financial Toxicity

Addressing out-of-pocket costs for drugs is critically important—particularly as drug prices rise and an increasing number of patients face coinsurance for their drugs—but it will not solve the problem of financial toxicity for cancer patients. Throughout the workshop series, the Panel heard and read many times about the overwhelming financial burden experienced by some cancer patients. Many patients—even those with health insurance—are unable to both cover their medical expenses and continue to pay for basic necessities. The scope of this problem goes beyond cancer drug costs, but the Panel believes that addressing financial toxicity is essential to ensuring that *all* patients achieve the best possible outcomes. Programs and resources that support cancer patients and their families are needed to prevent, detect, and address financial toxicity and ensure that costs do not exacerbate health inequities.

Financial Counseling Services

As recognition of financial toxicity has grown, many clinical settings, cancer programs, and nonprofit organizations have begun offering financial counseling services. Financial counselors may help patients navigate the complicated insurance landscape and identify external resources, including those that provide financial assistance for drugs. The increasing availability of financial counseling services is encouraging, but additional efforts are needed to ensure that information is provided in an effective manner and that the needs of all cancer patients are being met during and after treatment.

Patient Assistance Programs

Several types of programs offer financial assistance for cancer patients. Many pharmaceutical companies have programs that provide copay assistance or free drugs to patients. Other charitable organizations, such as those funded by private donations or grants, also help with treatment costs and indirect costs, such as transportation and lodging. Millions of U.S. cancer patients have received help from one or more of these programs. Concerns have been raised that some programs, particularly those sponsored by drug manufacturers, may increase spending on drugs by shielding patients from out-of-pocket expenses. The Panel shares this concern but believes that patient assistance programs should remain in place until alternative means are established to ensure access and prevent financial hardship. A shift toward value-based drug pricing and use should reduce the need for these programs.

Research to Better Prevent, Detect, and Address Financial Toxicity

Many unanswered questions remain regarding the best ways to meet patients' financial needs. Which patients are at highest risk of financial toxicity? Who should discuss costs with patients? Should people providing financial counseling receive specialized training? What types of cost information are most helpful to patients? At what points during the cancer care continuum should cost information be provided? How and when should tools to identify risk or presence of financial toxicity be integrated into clinical care? Cancer treatment facilities should monitor outcomes related to financial counseling services, and additional research should be done to identify the best ways to prevent, detect, and address financial toxicity among cancer patients.

Sources: Claxton G, Rae M, Panchal N. Consumer assets and patient cost sharing. Menlo Park (CA): The Henry J. Kaiser Family Foundation; 2015 Mar 11. Available from: http://www.kff.org/health-costs/issue-brief/consumer-assets-and-patient-cost-sharing; Association of Community Cancer Centers. 2016 trends in cancer programs. Rockville (MD): ACCC; 2016. Available from: http://www.accc-cancer.org/surveys/pdf/Trends-in-Cancer-Programs-2016.pdf; Zafar SY, Peppercorn JM. Patient financial assistance programs: a path to affordability or a barrier to accessible cancer care? J Clin Oncol. 2017;35(19):2113-6; Dafny LS, Ody CJ, Schmitt MA. Undermining value-based purchasing: lessons from the pharmaceutical industry. N Engl J Med. 2016;375(21):2013-5; Ubel PA, Bach PB. Copay assistance for expensive drugs: a helping hand that raises costs. Ann Intern Med. 2016;165(12):878-9.

Recommendation 4

Stimulate and maintain competition in the generic and biosimilar cancer drug markets.

The United States incentivizes innovation, in part by granting patents (property rights granted by the U.S. Patent and Trademark Office) and a number of exclusivities (delays and prohibitions on FDA approval of competitor drugs) to manufacturers of new drugs and biologics. These protections limit competition and increase potential for profit. Once relevant patents have expired (or been successfully challenged) and exclusivity ends, therapeutically equivalent generic drugs and biosimilars can be approved, creating potential for competition and possibly driving down prices. The Hatch-Waxman Act of 1984 established the current approval processes for generics and provided incentives for both brand-name and generic drug manufacturers. Since that time, the U.S. generic drug market has expanded dramatically—generic drugs accounted for 89 percent of retail prescriptions in 2016 compared with 19 percent in 1984.[129,130]

Use of generic oncology drugs saved the U.S. healthcare system an estimated $10 billion in 2016.

Generic drug prices are not a driver of the drug cost problem in the United States—while the average price for the most commonly used brand-name drugs has increased dramatically in recent years, prices of generic drugs have fallen by more than 70 percent since 2008.[131] The U.S. generic drug market saved the U.S. healthcare system an estimated $253 billion overall in 2016, including $10 billion in savings for oncology drugs.[129] Patients share in these savings as out-of-pocket costs are substantially lower for generics compared with brand-name drugs.[132] Use of low-cost generic drugs improves patient adherence to essential medication regimens and promotes better patient outcomes.[133] Unlike prices for brand-name drugs, which often are higher in the U.S. than in other countries,[134] prices for most generic drugs are lower in the United States than in Canada and Europe.[135,136]

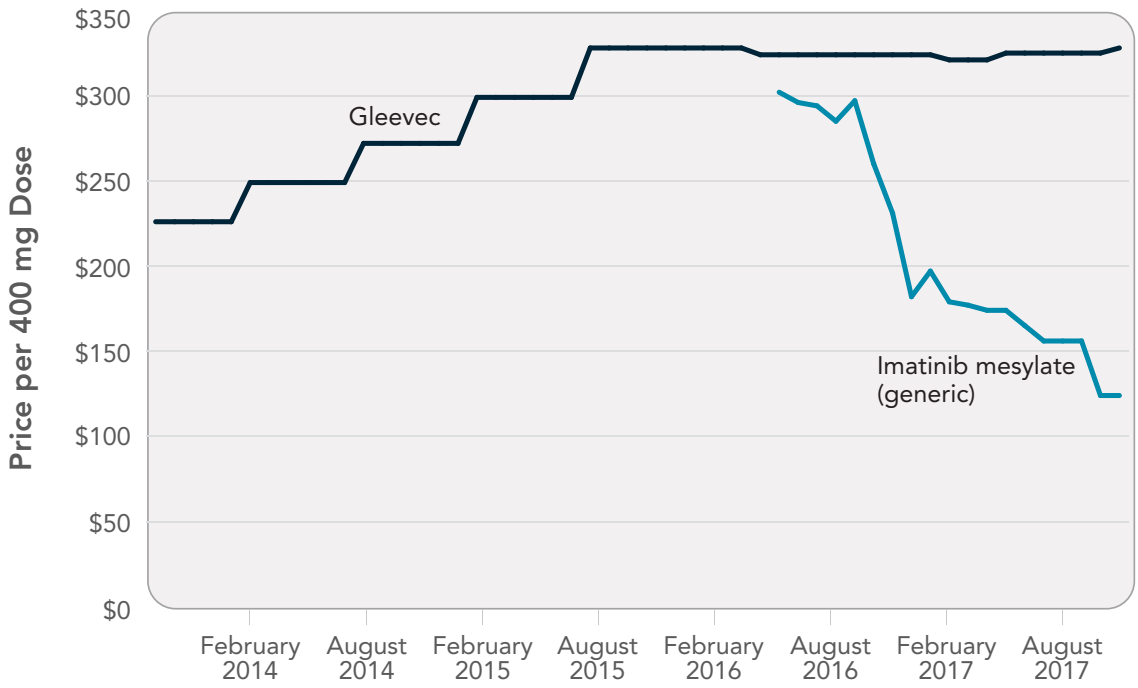
Consumers benefit most when generic drugs enter the market in a timely manner and there is healthy competition within the generic market to ensure low prices. In most cases, the first generic competitor is priced only slightly lower than its brand-name counterpart, but prices fall more—and are less likely to increase over time—when additional generics enter the market (see *Imatinib: Case Study of a Generic Cancer Drug* on page 22).[137,138] One study found that introduction of a second generic option reduced the average generic price to nearly half the price of the brand-name drug.[137] Insufficient competition may lead to higher prices, price spikes, and/or drug shortages, which have significant consequences for patients.[138-140] **Efforts must be made to facilitate timely and efficient market entry of generic and biosimilar drugs for cancer to bolster competition and ensure affordable access for patients.**

FDA Should Reduce Barriers to Market Entry for Generic Drugs and Biosimilars

FDA review and approval processes should facilitate timely market entry of generic drugs. Passage of the Hatch-Waxman Act spurred the submission of thousands of generic drug applications, which required review resources that exceeded FDA's funding for its Office of Generic Drugs, resulting in historically slow review processes.[141,142] The Generic Drug User Fee Amendments, enacted in 2012, provided additional resources for FDA to review the significantly increased number of generic drug applications and established targets for review of generic applications. Since that time, FDA has made progress on backlogged generic drug applications, achieved its target review times, and approved record high levels of generic drug applications.[141,142] FDA must continue to receive the resources it needs to review generic and biosimilar drug applications (Recommendation 5).

Imatinib: Case Study of a Generic Cancer Drug

Imatinib mesylate—brand name Gleevec—transformed treatment of chronic myeloid leukemia, restoring normal life expectancy for many patients who previously would have lived only a few years. Gleevec was priced at $26,000/year when it launched in 2001 and climbed to $146,000/year over the next 15 years. Although Gleevec's compound patent expired in July 2015, an agreement between the brand-name and generic manufacturers pushed back release of the first generic imatinib until February 2016. When the first generic was released, it was priced only slightly lower than Gleevec ($302 versus $324 per 400 mg tablet [National Average Drug Acquisition Cost]). Two additional generic versions of imatinib were released in August 2016, which put additional downward pressure on generic prices. The least costly option was $124 per tablet in November 2017, about $45,000 for a year of treatment. This is far less than Gleevec, but some patients still may need to pay hundreds of dollars every month for the drug.



Note: Graph shows National Average Drug Acquisition Cost, August 2013 to November 2017. **Sources**: Kantarjian H. The arrival of generic imatinib into the U.S. market: an educational event. The ASCO Post [Internet]. 2016 May 25 [cited 2017 Jun 23]. Available from: http://www.ascopost.com/issues/may-25-2016/the-arrival-of-generic-imatinib-into-the-us-market-an-educational-event; Langreth R. Popular cancer pill goes generic, yet patients' costs stay high. Bloomberg [Internet]. 2017 Jun 30. Available from: https://www.bloomberg.com/news/articles/2017-06-30/popular-cancer-pill-goes-generic-yet-patients-costs-stay-high; Centers for Medicare & Medicaid Services. NADAC (National Average Drug Acquisition Cost) [Internet]. Baltimore (MD): CMS; [cited 2017 Dec 22]. Available from: https://data.medicaid.gov/Drug-Pricing-and-Payment/NADAC-National-Average-Drug-Acquisition-Cost-/a4y5-998d/data

FDA also should reduce barriers for generic manufacturers to enter markets with no generic options or too few generic options to create competition. The recently launched Drug Competition Action Plan is a step in the right direction.[143] The Plan will further streamline the generic application review process and outlines several strategies for increasing competition in the generics market, including publication of a list of off-patent, off-exclusivity drugs without approved generics and expedited review of generic drug applications until there are three approved generics for a given drug product. The Plan also includes support for the development and approval of "complex" generic products. These are drugs—including some cancer treatments—having at least one feature that makes them harder to "genericize" under standard scientific and regulatory pathways.[144]

Regulators and Policy Makers Should Promote Healthy Competition in the Generic Drug Market

Several factors influence competition in the U.S. drug market. Generic drug makers decide whether to produce a drug based on potential for profit, which fluctuates based on factors such as supply and demand, manufacturing costs, availability of competitor products, and opportunities to shift their portfolios to more-profitable drugs.

The generic drug market has provided patients with affordable access to many drugs. In some cases, however, market forces or anticompetitive behaviors limit competition, which can lead to higher prices and/or drug shortages. For example, recent analyses suggest that generic competition for some cancer drugs may be suboptimal.[24,25] This may be due, in part, to smaller patient populations, which limit profit potential. Increasing consolidation of generic manufacturers also may diminish competition.[145] Reports also indicate that both brand-name and generic manufacturers use a variety of strategies to prevent or delay appropriate competition, costing consumers billions of dollars each year (see *Strategies Used to Delay or Limit Generic Drug Competition* on page 24).

Drug shortages, price spikes, and concerns about anticompetitive behaviors in the generic drug market have prompted investigation by Congress, the U.S. Department of Health and Human Services, and other federal agencies in recent years.[140,141,146] **U.S. regulatory agencies and policy makers should continue to monitor and evaluate the generic drug market to identify factors that prevent healthy competition. Deliberate efforts to limit competition must be addressed.** The Federal Trade Commission (FTC) should continue to consider the impact of mergers and acquisitions on competition. FTC and the U.S. Department of Justice should continue investigating potential anticompetitive behavior by brand-name and generic drug companies—including pay-for-delay settlements and price fixing—and ensure that offenders are held responsible. FDA also should continue to examine ways in which it can help curb practices—such as inappropriate use of citizen petitions and limiting distribution of drug samples for bioequivalence testing—that reduce competition.

Emerging Biosimilars Market Should Be Monitored

The rising cost of cancer drugs over the past several years has been driven largely by high-priced biological products, or "biologics," which are products isolated from living organisms or systems.[3] Patents for some cancer biologics have expired and many more will expire over the next few years, raising hopes that biosimilars—like generic drugs—will provide financial relief. Biosimilars are products that are highly similar to and have no clinically meaningful differences from an existing FDA-approved product. However, biologic products, including biosimilars, are far more difficult and expensive to develop and manufacture than other drugs, making it difficult to predict cost savings. Lower costs and increased patient access to biologics have occurred in Europe, where nearly 30 biosimilars have been approved since 2006.[147] The U.S. biosimilars market has emerged more slowly. An abbreviated pathway for biosimilar approval was created by the Biologics Price

Strategies Used to Delay or Limit Generic Drug Competition

Pay-for-delay (reverse settlement payments): Manufacturers of brand-name drugs pay or provide other compensation (e.g., agree not to market an authorized generic) to generic drug companies to delay introduction of competitor generics. This costs U.S. consumers and taxpayers an estimated $3.5 billion per year.

Citizen petitions: Individuals and/or organizations can ask FDA to delay action on a pending generic drug application. The process is intended to identify legitimate scientific and regulatory concerns about a drug, but the process often is exploited by brand-name drug companies attempting to delay competition.

Limiting distribution of drug samples for bioequivalence testing: To obtain approval for a generic drug, companies must demonstrate that their products are bioequivalent to the brand-name drugs. Often, this requires that a generic drug developer purchase physical samples of the brand-name reference drug. As of July 2017, FDA had received more than 150 inquiries from generic drug companies that were unable to access samples for testing.

Patent "evergreening" (product hopping): Some companies reformulate their brand-name drugs and encourage physicians to prescribe the new formulation. In some cases, the older drug may even be removed from the market. In addition, the new formulation may itself be protected from competition by patents and/or exclusivities. In addition, as a result of these activities, generic substitution of the original formulation may be made more difficult or impossible.

Price fixing: Generic drug manufacturers agree to a certain price or price range—usually higher than market forces would allow—for their respective competing generic drugs.

Sources: U.S. Department of Health and Human Services Office of the Assistant Secretary for Planning and Evaluation. ASPE Issue Brief: Understanding recent trends in generic drug prices. Washington (DC): ASPE; 2016 Jan 27. Available from: https://aspe.hhs.gov/system/files/pdf/175071/GenericsDrugpaperr.pdf; Federal Trade Commission. Authorized generic drugs: short-term effects and long-term impact: a report of the Federal Trade Commission. Washington (DC): FTC; 2011 Aug. Available from: https://www.ftc.gov/reports/authorized-generic-drugs-short-term-effects-long-term-impact-report-federal-trade-commission; Carrier MA. Citizen petitions: long, late-filed, and at-last denied. Am Univ Law Rev. 2017;66(2): Article 1. Available from: http://digitalcommons.wcl.american.edu/aulr/vol66/iss2/1; Carrier MA, Wander D. Citizen petitions: an empirical study. Cardozo Law Rev. 2012;34:249-93. Available from: http://cardozolawreview.com/content/34-1/Carrier.34.1.pdf; Gottlieb S. Antitrust concerns and the FDA approval process (statement before the U.S. House Committee on the Judiciary, Subcommittee on Regulatory Reform, Commercial and Antitrust Law). Washington (DC): U.S. House of Representatives; 2017 Jul 27. Available from: https://www.fda.gov/NewsEvents/Testimony/ucm568869.htm; Carrier MA, Shadowen SD. Product hopping: a new framework. Notre Dame Law Rev. 2016 Nov;92(1): Article 4. Available from: http://scholarship.law.nd.edu/cgi/viewcontent.cgi?article=4680&context=ndlr; Kesselheim AS. Intellectual property policy in the pharmaceutical sciences: the effect of inappropriate patents and market exclusivity extensions on the health care system. AAPS J. 2007;9(3):E306-11; Thomas K. 2 former drug executives charged with price fixing. The New York Times [Internet]. 2016 Dec 14 [cited 2017 Aug 29]. Available from: https://nyti.ms/2jR2Iqv; Thomas K. 20 states accuse generic drug companies of price fixing. The New York Times [Internet]. 2016 Dec 15 [cited 2017 Aug 29]. Available from: https://nyti.ms/2k6j5iH

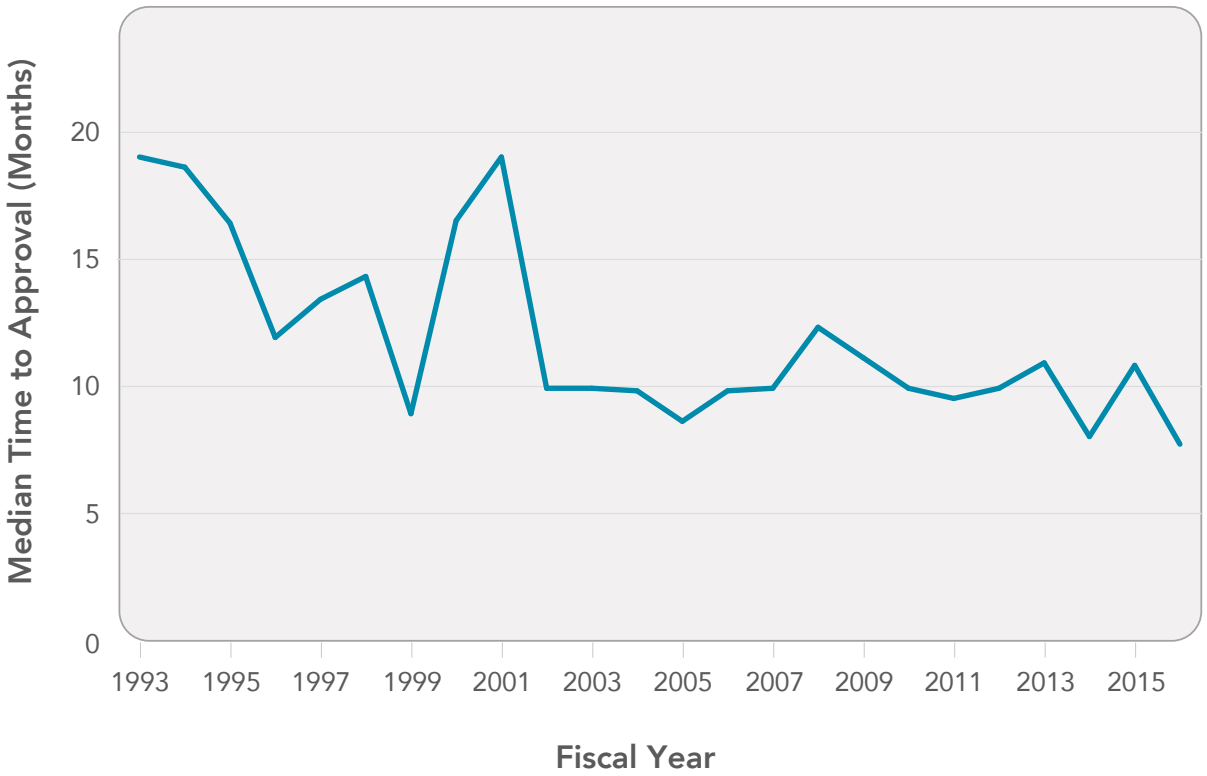
Competition and Innovation Act of 2009, and FDA has issued several guidance documents for industry to support the development of biosimilars.[148] The first two biosimilars for the treatment of cancer—one for bevacizumab (Avastin) and one for trastuzumab (Herceptin)—were recently approved,[149,150] and others are under development.[151] **FDA should continue to monitor the emerging U.S. biosimilars landscape and ensure that approval processes and manufacturing oversight are functioning efficiently such that biosimilar products can be made available to the American public.** Whenever appropriate, lessons on biosimilar regulation should be gleaned from the European Medicines Agency.

Recommendation 5

Ensure that the FDA has appropriate resources to assess cancer drug safety and efficacy efficiently.

The U.S. Food and Drug Administration plays a critical role in ensuring patient access to innovative cancer drugs. FDA has been characterized by some as "slow and burdensome,"[152] but these claims are unwarranted. FDA reviews and approves drugs more quickly than its European counterpart[153] and has cut review times in half over the past 25 years (Figure 5).[154] Cancer drugs are no exception—half of new drug applications for cancer treatments approved by FDA between 2003 and 2016 were approved within six months, and virtually all were approved within one year.[155]

Figure 5. FDA Median Time to Approval for New Drug Applications and Biologics License Applications, Fiscal Years 1993-2016



Source: Jenkins JK. CDER new drug review: 2016 update. Presented at: FDA/CMS Summit; 2016 Dec 14; Washington, DC. London (UK): Informa Life Sciences. Available from: https://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM533192.pdf

Cancer drug development and evaluation present distinct challenges, particularly in the age of precision medicine. FDA has implemented policies and programs to address many of these challenges. The Oncology Center of Excellence was established to enable more efficient and effective review of cancer treatments (see *FDA Oncology Center of Excellence* on page 27).[156] The Panel supports the efforts of the Center. The agency also has implemented various programs, including breakthrough therapy designation, that allow it to focus resources on particularly promising new drugs to treat serious conditions that may demonstrate substantial improvement over existing therapies.[157] In some cases, these programs have helped patients gain earlier access to effective new drugs.[158]

The Panel urges the President and Congress to ensure that the FDA has the resources and authority to assess the safety and efficacy of oncology products and to appropriately staff the Oncology Center of Excellence. Adequate resources also are needed to conduct postapproval drug safety monitoring, ensure that foreign and domestic manufacturing facilities adhere to safety and quality standards, and enable efficient review of both novel and generic/biosimilar drugs (Recommendation 4).

An adequately staffed and well-resourced FDA is more important than ever in the modern era of oncology product development. Innovative trial designs—such as seamless expansion cohort designs and platform trials—are being developed to evaluate emerging cancer treatments, including molecularly targeted therapies, immunotherapies, and combination therapies. Such trials enable adequate safety and efficacy testing with fewer patients and shorter timeframes than traditional randomized controlled trials. The Panel heard from many stakeholders that FDA regulators and statisticians are at the forefront of clinical trial design and statistical analysis and, as such, are essential assets to cancer product development.

A highly skilled FDA workforce also is essential as the agency considers important questions about incorporation of new kinds of data into its review processes. As directed in the 21st Century Cures Act[159] and the FDA Reauthorization Act (FDARA),[160] FDA also is working to enhance the patient voice in drug development. The Oncology Center of Excellence is contributing to these efforts through its Patient-Focused Drug Development program (see *FDA Oncology Center of Excellence* on page 27). The Panel commends FDA's efforts to incorporate patients' perspectives and experiences in the drug testing and regulatory review process and looks forward to continued commitment to patient-focused drug development.

The 21st Century Cures Act and FDARA also charge the Secretary of the U.S. Department of Health and Human Services and FDA with exploring use of real-world evidence—defined as data from sources other than traditional trials[159]—in regulatory decision making. Some have expressed concern that this could lead to less rigorous review.[161] The Panel agrees it is critical that FDA continue to demand rigorous science for the demonstration of both safety and efficacy. Real-world evidence has potential to offer valuable insights based on how drugs are used and work in clinical settings (see the Panel's 2016 report *Improving Cancer-Related Outcomes with Connected Health*). It is important, however, to ensure that data limitations are well characterized and accounted for in statistical analyses and interpretation. Future guidance from FDA on use of real-world evidence should reflect these considerations.

FDA Oncology Center of Excellence

The FDA Oncology Center of Excellence was created in 2016 as part of the Cancer Moonshot with the goal of expediting the development of oncology and hematology medical products. The Center brings together regulatory scientists and reviewers with expertise in drugs, biologics, devices, and data science to support an integrated approach to evaluation of products for the diagnosis and treatment of cancer.

One of the Center's key efforts is the Patient-Focused Drug Development program. The overarching goal of the program is to identify rigorous methods to assess patients' experiences to inform evaluation of cancer drugs. Key activities include engaging with patients and patient advocacy groups, fostering research into measurement of patients' experiences, and generating science-based recommendations for regulatory policy.

Recommendation 6

Invest in biomedical research to create a strong foundation for developing innovative, high-value cancer drugs.

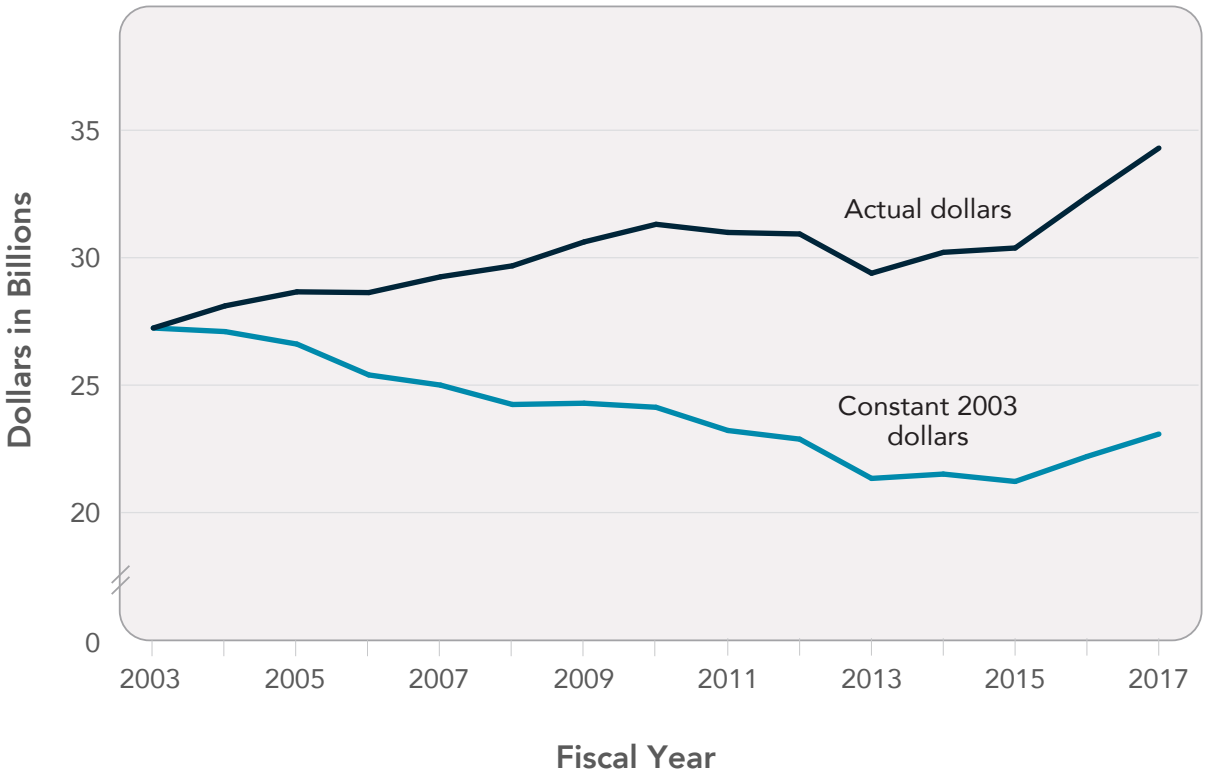
A strong research infrastructure and workforce are essential to develop and deploy innovative, high-value drugs that potentially cure or, if not cure, significantly extend and improve the lives of cancer patients. The U.S. has long been a leader in biomedical research and pharmaceutical innovation, in large part because of cross-sector investment by government, industry, and nonprofit organizations.[162] A vibrant discovery ecosystem is essential to ensure that the cancer drug pipeline continues to produce high-value products that benefit all patients.

NIH—with an annual budget of nearly $32.3 billion[163]—is the world's leading funding organization for biomedical research.[164] The basic, translational, clinical, and population sciences research carried out by NIH-supported investigators has helped elucidate the molecular underpinnings of several cancer types and contributed to development of novel therapies—such as imatinib (Gleevec) and ipilimumab (Yervoy)—that have dramatically improved outcomes for patients. In addition to contributing to the development of new drugs, NIH also conducts clinical trials to determine the best ways to use drugs in real-world settings; for example, the National Cancer Institute Molecular Analysis for Therapy Choice Trial (NCI-MATCH)—which is being carried out by collaborators across the country—is testing the effectiveness of several cancer drugs in patients with specific mutations.[165] These efforts and others have been driven by the creativity and hard work of numerous researchers, including many who immigrated to the United States. In addition, NIH training grants and career development programs play a critical role in building the U.S. biomedical research workforce.

The NIH budget has not kept pace with inflation since 2003.

NIH historically has enjoyed bipartisan congressional support, most recently demonstrated by passage of the 21st Century Cures Act, which provides NIH with a bolus of additional funding for special initiatives such as the Precision Medicine Initiative and the Cancer Moonshot.[166] Pharmaceutical companies also have emphasized the critical role of NIH in funding the types of early-stage research that their companies cannot do.[167] However, over the past 15 years, the NIH

Figure 6. NIH Appropriations, Fiscal Years 2003-2017



Source: Federation of American Societies for Experimental Biology. NIH research funding trends [Internet]. Bethesda (MD): FASEB; [updated 2017 Jun 26; cited 2017 Oct 6]. Available from: http://faseb.org/Science-Policy-and-Advocacy/Federal-Funding-Data/NIH-Research-Funding-Trends.aspx

budget has not kept pace with inflation (Figure 6). Despite budget increases in the past two fiscal years, NIH's capacity to support research remains far below 2003 levels. **The Panel urges the President and Congress to provide sustained, predictable funding for NIH that, at a minimum, keeps pace with inflation. NIH funding is essential to the National Cancer Program and will lay the foundation for development of innovative drugs that provide high value to cancer patients**. Failure to invest in NIH will threaten the United States' role as a global leader in the biomedical sciences and future progress against cancer.

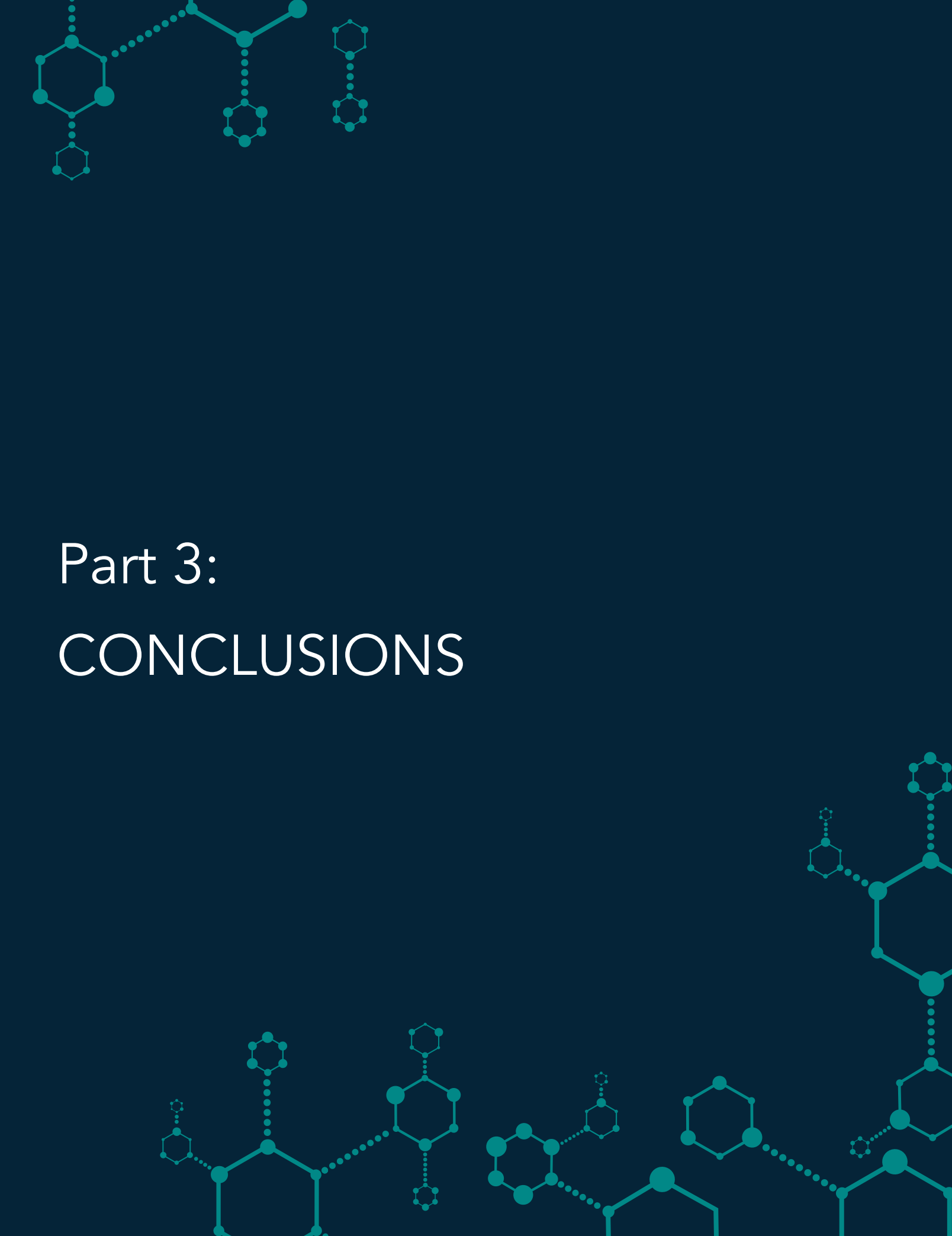
The Panel also urges continued commitment to cancer research by other sectors, including nonprofit organizations, venture capital companies, and the biopharmaceutical industry. Sustained investment from multiple sectors is needed to build and maintain a pipeline of oncology drugs that provide transformative rather than incremental benefits. Biopharmaceutical companies play a particularly critical role in conducting clinical trials necessary to determine the safety and efficacy of new drugs and drug combinations. U.S. laws, regulations, and policies should encourage investments in cancer research and drug development.

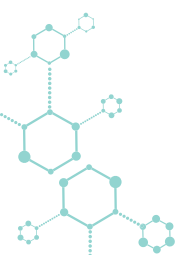
As noted in recent reports from the Panel[109] and the Cancer Moonshot Task Force,[110] a culture of collaboration is essential for catalyzing new scientific breakthroughs. There are many opportunities for stakeholders to work together, including:

- Increasing availability of drugs for preclinical research to gain insights into mechanisms of action and potential biomarkers;
- Sharing data, including clinical trial outcomes, to inform future research;
- Collaborating to test promising combination therapies, including combinations of drugs manufactured by different companies; and
- Engaging patients and patient advocates to ensure that research is aligned with patients' needs and priorities.

Though cross-sectional collaborations and partnerships can be challenging, researchers, research-funding organizations, biopharmaceutical companies, and patients should find ways to work together to accelerate development of innovative new cancer drugs that will extend and improve patients' lives. Some efforts are under way to facilitate these types of collaboration. One example is the National Cancer Institute agent formulary (NCI Formulary),[168] a public-private partnership between NCI and biopharmaceutical companies that provides NCI-designated Cancer Center investigators rapid access to agents for cancer clinical trial use or preclinical research. Additional initiatives and platforms that facilitate collaboration should be established and supported.

Part 3:
CONCLUSIONS





Innovative cancer drugs offer new hope for cancer patients, including opportunities for improved quality of life and long-term survival, even cure. However, oncology drug costs are increasing far more rapidly than costs of other components of cancer care. Virtually all new cancer drugs enter the market with a price tag higher than $100,000 per year, and increasing numbers of patients are being treated with these high-priced new drugs. Use of drug combinations may exacerbate the problem dramatically. Faced with staggering out-of-pocket costs for drugs and other components of cancer care, some patients suffer financial toxicity or forego needed treatment, which may shorten survival.

Urgent action is needed to address ongoing, rapid increases in cancer drug costs while continuing to stimulate innovation in drug development. This complex problem will not be solved quickly or easily, and it will not be solved by any organization or sector working alone. Proposed strategies and policies should be tested to ensure effectiveness in real-world settings and to minimize negative, unintended consequences; moreover, impact on the total cost of cancer care must be considered. Efforts to address drug costs should adhere to the guiding principles listed below.

Cancer drug prices should be aligned with value to patients. Prices of new cancer drugs entering the market are now uniformly high, regardless of novelty or clinical efficacy. High prices should be reserved for transformative, highly effective drugs. A foundational step toward this pricing approach is to develop and adopt a widely accepted framework for assessing the value of cancer drugs. Though value has many components, benefits experienced by patients must be central to any framework. Transparency and clear communication are essential to ensure that patients have all the information they need—including on potential benefits and side effects, as well as costs—to enable them to choose which treatment option best reflects their needs, values, and preferences.

All patients should have affordable access to appropriate cancer drugs. High-quality cancer care—including the most appropriate branded and/or generic drugs—should be accessible to all patients without the threat of financial toxicity. High-quality health insurance with prescription drug coverage is essential for limiting out-of-pocket costs. Very few uninsured or underinsured patients could afford to pay full price for cancer drugs, particularly the innovative new drugs entering the market. Improvements in health insurance coverage achieved over the past few years in the United States should be expanded, not reversed. Ability to pay should not be the predictor of who lives and who dies.

Investments in science are essential to drive future innovation. Biomedical research is the foundation of innovative drug development. Continued advances in cancer treatments depend on steadfast support for basic, translational, clinical, and population sciences research. Investments in regulatory science and infrastructure are essential to accelerate patients' access to innovative drugs by ensuring that drugs are efficiently and effectively evaluated, both before and after market entry. Developers of innovative drugs also should be financially rewarded to incentivize and support future innovation. These steps will help ensure that future drugs have transformational, not incremental, impact.

Rising cancer drug costs are unprecedented and cannot be ignored—the consequences for patients, families, and society are too great. If current trends continue, spending on drugs will undermine ability to pay for other healthcare needs or invest in other critical priorities, like education and infrastructure. More than ever, affordable access to drugs will be the difference between life and death for cancer patients. **The Panel urges all stakeholders—drug developers and manufacturers, policy makers, government, public and private payers, healthcare institutions and systems, providers, and patients—to work together to ensure that patients have access to innovative, high-value, and affordable cancer drugs.** The ultimate goal is to ensure that patients receive high-quality cancer treatment and experience the best possible health outcomes without financial toxicity.

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APPENDIX A: WORKSHOP DATES AND ROSTER OF PARTICIPANTS

MEETING DATE	LOCATION
July 10, 2016	New York, NY
December 9, 2016	Arlington, VA
March 27, 2017	Philadelphia, PA

MEETING PARTICIPANTS	AFFILIATIONS
Erin Aakhus, MD	University of Pennsylvania
Julian Adams, PhD	Infinity Pharmaceuticals
Margaret Anderson, MSc	*FasterCures*
Peter Bach, MD	Memorial Sloan Kettering Cancer Center
Anthony Barrueta, JD	Kaiser Foundation Health Plan, Inc.
Roy Baynes, MD, PhD	Merck & Co., Inc.
Donald Berry, PhD	The University of Texas MD Anderson Cancer Center
Heather Block	Breast Cancer Patient and Advocate
Carmella Bocchino, RN	America's Health Insurance Plans
Randy Burkholder	PhRMA
Danielle Carnival, PhD	White House Cancer Moonshot Task Force
Frank Clyburn, MBA	Merck & Co., Inc.
Jason Cristofaro, JD, PhD	National Cancer Institute
Deanna Darlington	Amgen, Inc.
Kathleen Denis, PhD	The Rockefeller University
Stacie Dusetzina, PhD	University of North Carolina at Chapel Hill
Shelley Fuld Nasso, MPP	National Coalition for Cancer Survivorship
Levi Garraway, MD	Eli Lilly and Company
Ann Geiger, PhD, MPH	National Cancer Institute
Gary Gilliland, MD, PhD	Fred Hutchinson Cancer Research Center
Hadiyah-Nicole Green, PhD	Ora Lee Smith Cancer Research Foundation
Hill Harper, JD	President's Cancer Panel Author, Actor, and Philanthropist
Clifford Hudis, MD, FACP	American Society of Clinical Oncology Memorial Sloan Kettering Cancer Center
Suleika Jaouad	*New York Times* Columnist Young Adult Cancer Advocate
Scott Josephs, MD	Cigna

MEETING PARTICIPANTS	AFFILIATIONS
Aaron Kesselheim, MD, JD	Brigham and Women's Hospital Harvard Medical School
Ron Kline, MD	Centers for Medicare & Medicaid Services
Paul Kluetz, MD	U.S. Food and Drug Administration
David Lansky, PhD	Pacific Business Group on Health
Lisa LaVange, PhD	U.S. Food and Drug Administration
Sharon Levine, MD	The Permanente Federation, Kaiser Permanente The Permanente Medical Group of Northern California
Kim Marschhauser, PhD	Patient-Centered Outcomes Research Institute
Steve Miller, MD	Express Scripts
Lori Minasian, MD	National Cancer Institute
Meg Mooney, MD	National Cancer Institute
Lee Newcomer, MD	UnitedHealthcare
Jeremy Nobel, MD	Northeast Business Group on Health Harvard Medical School
Loyce Pace, MPH	LIVESTRONG Foundation
Richard Pazdur, MD	U.S. Food and Drug Administration
Caroline Pearson	Avalere Health
Vinay Prasad, MD, MPH	Oregon Health & Science University
Scott Ramsey, MD, PhD	Fred Hutchinson Cancer Research Center
Barbara Rimer, DrPH	President's Cancer Panel University of North Carolina at Chapel Hill
Meredith Rosenthal, PhD	Harvard T.H. Chan School of Public Health
Mace Rothenberg, MD	Pfizer, Inc.
Abby Sandler, PhD	President's Cancer Panel National Cancer Institute
Ameet Sarpatwari, JD, PhD	Brigham and Women's Hospital Harvard Medical School
Frederic Sax, MD	Quintiles Advisory Services
George Scangos, PhD	Biogen
Andrew Schorr, MS	Patient Power, LLC
Greg Simon, JD	Biden Cancer Initiative
Josephine Sollano, PhD, MPH	Pfizer, Inc.
Philip Stella, MD	St. Joseph Mercy Hospital-Ann Arbor
Owen Witte, MD	President's Cancer Panel University of California, Los Angeles
Yousuf Zafar, MD	Duke Cancer Institute
James Zwiebel, MD	National Cancer Institute

APPENDIX B: PANEL RECOMMENDATIONS AND RESPONSIBLE STAKEHOLDERS

A broad set of stakeholders must contribute to efforts to align cancer drug prices with their value, ensure affordable access to cancer drugs for all patients, and promote future innovation in cancer drug development. This table identifies stakeholders (listed alphabetically) that could play important roles in implementing the Panel's recommendations to achieve these goals. Stakeholder lists are not necessarily exhaustive. Further, inclusion in this table does not indicate endorsement of the Panel recommendations.

RECOMMENDATION	RESPONSIBLE STAKEHOLDERS
1. Promote value-based pricing and use of cancer drugs.	Biopharmaceutical companies Center for Medicare & Medicaid Innovation Federal and state policy makers Healthcare providers Healthcare systems Institute for Clinical and Economic Review Medicare Payment Advisory Commission National Academies of Sciences, Engineering, and Medicine National Association of Insurance Commissioners Patients, families/caregivers, and patient advocacy organizations (e.g., Patient Power, NCCS, LIVESTRONG Foundation, *FasterCures*) Pharmaceutical supply chain organizations (e.g., pharmacy benefit managers, wholesalers, retailers) Professional associations (e.g., ASCO, AHIP) Public and private payers
2. Enable meaningful communication about treatment options, including cost information, to support patients' decision making.	Center for Medicare & Medicaid Innovation Federal and state policy makers Healthcare providers Healthcare systems National Comprehensive Cancer Network Patients, families/caregivers, and patient advocacy organizations (e.g., Patient Power, NCCS, LIVESTRONG Foundation, *FasterCures*) Professional associations (e.g., ASCO, ONS) Public and private payers Research funding organizations (NIH/NCI, DoD, PCORI, nonprofit/advocacy organizations [e.g., ACS]) Researchers

RECOMMENDATION	RESPONSIBLE STAKEHOLDERS
3. Minimize the contributions of drug costs to financial toxicity for cancer patients and their families.	Cancer care teams Congress Healthcare systems Medicare Payment Advisory Commission Patients, families/caregivers, and patient advocacy organizations (e.g., Patient Power, NCCS, LIVESTRONG Foundation) President Public and private payers Research funding organizations (e.g., NIH/NCI, nonprofit/advocacy organizations [e.g., ACS]) Researchers Secretary of the U.S. Department of Health and Human Services
4. Stimulate and maintain competition in the generic and biosimilar cancer drug markets.	Biopharmaceutical companies Congress Federal Trade Commission U.S. Department of Health and Human Services U.S. Department of Justice U.S. Food and Drug Administration and FDA Commissioner
5. Ensure that FDA has appropriate resources to assess cancer drug safety and efficacy efficiently.	Congress President
6. Invest in biomedical research to create a strong foundation for developing innovative, high-value cancer drugs.	Academic institutions Biopharmaceutical companies Congress President Research advocacy organizations (e.g., AAAS, AAMC, Research!America, *FasterCures*) Research funding organizations (NIH/NCI, DoD, nonprofit/advocacy organizations, [e.g., ACS]) Researchers Venture capital companies

Note: AAAS = American Association for the Advancement of Science, AAMC = Association of American Medical Colleges, ACS = American Cancer Society, AHIP = America's Health Insurance Plans, ASCO = American Society of Clinical Oncology, DoD = U.S. Department of Defense, FDA = U.S. Food and Drug Administration, NCCS = National Coalition for Cancer Survivorship, NCI = National Cancer Institute, NIH = National Institutes of Health, ONS = Oncology Nursing Society, PCORI = Patient-Centered Outcomes Research Institute

APPENDIX C: ACRONYMS

ACRONYM	DEFINITION
AAAS	American Association for the Advancement of Science
AAMC	Association of American Medical Colleges
ACS	American Cancer Society
AHIP	America's Health Insurance Plans
APM	Alternative payment model
ASCO	American Society of Clinical Oncology
CMS	Centers for Medicare & Medicaid Services
DoD	U.S. Department of Defense
FDA	U.S. Food and Drug Administration
FDARA	FDA Reauthorization Act
FTC	Federal Trade Commission
ICER	Institute for Clinical and Economic Review
NASEM	National Academies of Sciences, Engineering, and Medicine
NCCS	National Coalition for Cancer Survivorship
NCI	National Cancer Institute
NIH	National Institutes of Health
OCM	Oncology Care Model
ONS	Oncology Nursing Society
PCORI	Patient-Centered Outcomes Research Institute
VBID	Value-based insurance design

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