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Small Molecule Medicines: Why They're Vital for Patients

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Medicines are central to the diagnosis, cure, treatment and prevention of many illnesses.[1] They are classified as two types: small molecule medicines and large molecule (or biologic) medicines.[2]

Small molecule medicines are what most people think of when they imagine a medicine. They are chemically synthesized drugs that are typically taken in oral form. Millions of Americans take small molecule medicines like statins to lower cholesterol, metformin to lower blood sugar or antibiotics to treat a range of infections.

Biologic medicines, on the other hand, are made from living cells, are structurally much more complex than small molecule medicines and are most often injected or infused in a doctor's office or hospital setting. Examples of biologic medicines include immunotherapies which enlist the immune system to fight cancer, and monoclonal antibodies which are used in the treatment of a range of autoimmune conditions and many other illnesses.

Both biologic medicines and small molecule medicines serve specific purposes that are essential to the treatment of different diseases in unique ways. As a result, they are both indispensable in providing patients, caregivers and health care providers with the tools necessary to achieve certain therapeutic effects in patients.

As small molecules account for the majority of novel medicines approved by the U.S. Food and Drug Administration (FDA)—representing three-quarters approved in recent years—the impact they have on the treatment of various health conditions is particularly important.[3] That is due in part to their clinical characteristics which include their ability to reach therapeutic targets that are inside of cells as well as their ability to cross the blood-brain barrier into the brain. These features allow them to play a central role in the treatment of many health conditions—including those commonly impacting older, disabled and chronically ill populations, such as cancers, psychiatric conditions, diseases impacting the central nervous system and many more. Small molecule medicines also provide significant flexibility to meet a wide range of patient needs and offer great convenience to patients, caregivers and health care providers. These features in turn reduce barriers to patient access and adherence while also reducing factors which can drive health disparities.

This paper highlights the key benefits of small molecule medicines to patients and our health care system and underscores the importance of encouraging continued research and development (R&D) of these medicines.

IRA Discourages Investment in Small Molecule Medicines by Setting an Arbitrarily Short Timeline Before Eligibility for Government Price Setting

Despite the important advantages small molecule medicines offer in the treatment of many illnesses, government price-setting provisions in the recently passed Inflation Reduction Act (IRA) could result in fewer of these medicines coming to market in the future. The IRA's drug price-setting provisions explicitly reduce incentives for small molecule R&D investments compared to biologic medicines by allowing eligible small molecule medicines covered by Medicare to be selected for price setting four years earlier than biologics. Small molecule medicines can be selected for price setting a mere seven years after initial FDA approval with the set price effective at year nine, which is substantially shorter than the current effective patent life of 13 to 14 years for these medicines.[4] Biopharmaceutical companies are already taking the law into account when making tough decisions about their R&D projects. In a survey of biopharmaceutical companies, 63% said they expect to shift R&D investment away from small molecule medicines and toward biologic medicines as a result of the law.[5]

Not only does the law discourage investment in small molecule medicines, but because it impacts medicines covered by Medicare, it also has a chilling effect on the development of medicines that treat elderly and disabled patients. In fact, the same survey found at least 82% of biopharmaceutical companies with pipeline projects in cardiovascular disease, mental health, neurology, infectious disease and cancer[6], expect substantial impacts on R&D decisions in these areas. Small molecules play a critical role in treating each of these disease areas and treatments for these illnesses often affect patients whose prescriptions are covered under Medicare.

Small Molecule Medicines Offer Unique Clinical Benefits

Medicines typically target proteins associated with a specific biological process that, when not functioning properly, cause disease. To treat disease, a medicine must be able to reach a specific therapeutic target.[7] In some cases, medicines target proteins that are found outside or on the surface of cells, but in other cases, these targets are inside the cell.

Small Molecule Medicines Can Reach Therapeutic Targets Inside of Cells

The distinction between medicine targets that are on the cell surface and those that are inside cells is important because cell membranes are "selectively permeable" in that they do not allow all substances–including some medicines–to pass through to reach the interior of the cell. This feature of cell membranes protects the cell from the effects of harmful substances in the extracellular environment, but it also creates challenges for scientists seeking to develop medicines for diseases that are associated with target proteins inside the cell.

The molecular weight of medicines impacts how they are developed to reach specific therapeutic targets, which routes (oral, injection, inhaled, etc.) can be used to administer a medicine to patients and how much of the medicine patients need to take to receive therapeutic benefit. Compared to biologic medicines, small molecule medicines have simpler structures, low molecular weight and the ability to cross cell membranes with relative ease. These characteristics make it easier for small molecule medicines to reach their therapeutic targets inside cells to facilitate clinical benefit.

Due to the ability of small molecule medicines to penetrate cell membranes and reach therapeutic targets, including the cell's inner machinery where many targets are located, the importance of these medicines in the treatment of many diseases cannot be overstated.

Illustrating the Importance of Cell Permeability in the Treatment of Disease

Metformin is recommended as first-line treatment for Type 2 diabetes and is the most widely used medication to treat it. Metformin targets an enzyme called AMPK, which is found in the nucleus and cytoplasm of the cell, both of which are located inside the cell. The ability of metformin to target AMPK is due in part to its small molecular size and ability to cross the cell membrane. The importance of small molecule medicines like metformin to the more than 37 million people in the United States with Type 2 diabetes is substantial, particularly given the high prevalence and cost of this condition.[8,9] Metformin is only one of many small molecule medicines that treat highly prevalent, life-threatening conditions whose mechanism of action leverages its ability to cross the cell membrane.

Case Study: Small Molecule Medicines Capable of Targeting Mechanisms Inside Cancer Cells Drive Critical Treatment Advances for Cancer Patients

Small molecule medicines have emerged as a critical part of the treatment arsenal against cancer, due in large part to the ability of these medicines to reach medicine targets inside cells, where cancer originates. Cancer begins with a gene mutation, which is a change in a cell's DNA that interrupts normal cellular function. Genes instruct cells about how to make certain proteins that control normal cellular function. Cancer-causing gene mutations change how these proteins are produced, and these changes make cells divide more than they should, eventually resulting in the development of cancer.[10]

As more is learned about the molecular and genetic underpinnings of cancer, a greater understanding has emerged about gene mutations that create proteins that send signals telling cancer cells to divide and spread. This understanding has led to a remarkable shift in the approach to cancer treatment. Historically, cancer was often treated with chemotherapy medicines that indiscriminately target all actively dividing cells. Although chemotherapies are often effective and these medicines continue to be broadly used today, because of their less targeted action these treatments can also be associated with significant side effects such as hair loss, nausea and vomiting.

In recent years, an improved understanding of the genetic basis of cancer in particular has led to the development of medicines that directly target the mechanisms that drive cancer cell growth, while sparing normal cells. Small molecule targeted therapies are uniquely capable of achieving this dual goal because they are small enough to enter cells and designed to target specific processes within them that drive cancer cells to divide and spread.

Small molecule targeted cancer medicines work through numerous mechanisms that:

- **Cause cancer cells to die**
- **Interrupt signals that tell cancer cells to divide**
- **Block growth of blood vessels which are necessary to support tumor growth**
- **Prevent cancer cells from receiving hormones they need to grow**

These medicines offer enormous benefits to patients and health care providers because doctors can select treatments that target specific characteristics of an individual patient's cancer cells–including increasingly the genetic characteristics. They are also convenient to patients because they are taken orally and reduce the need for patients to travel to receive infusions. As a result of these features, it is not surprising that over the past 20 years there has been a significant increase in FDA-approved targeted small molecule cancer medicines, and today, a majority of cancer medicines approved are small molecule medicines.[11] In fact, between 2001 and 2020, 89 unique targeted small molecule medicines have been approved by the FDA, many approved for multiple types of cancer, evidencing a complete paradigm shift in treatment capable of addressing the genetic changes that lead to cancer cell growth.[12]

One of the first classes of these therapies to become available to cancer patients, tyrosine kinase inhibitors (TKIs), illustrates the benefits that small molecule targeted therapies can provide across a range of cancers. FDA approved the first TKI in 2001 for treatment of chronic myelogenous leukemia (CML). This therapy targets the abnormal BCR-ABL1 protein inside cancer cells. This mutation stems from the fusion of two genes that causes uncontrolled proliferation of white blood cells which leads to this form of leukemia.[13] Before TKIs were approved for CML, 10-year survival with this cancer was approximately 20%, but it increased to 85% with TKI treatment.[14] Today, patients with CML can expect to live close to normal life spans. This is due in large part to initial TKI therapy and the approval of additional TKIs that provide critical options for CML patients whose tumors develop resistance to initial targeted treatment.[15]

The benefits of small molecule TKI therapy have also expanded beyond CML to other cancers. For example, because the same gene mutation in CML is also found in 20% of patients with acute lymphocytic leukemia (ALL), TKIs have also changed the treatment landscape for patients with ALL. Beyond leukemias, this class of medicines has also been developed to target at least 12 different pathways that allow cancer to grow and spread in other tissues and organs–including breast, stomach, lung, colon, liver, thyroid and kidney cancers. The importance of this class of small molecule medicines in targeting specific genetic mutations for patients across a wide range of cancers is just one example of the invaluable contributions that small molecule targeted therapies have made to the cancer treatment arsenal in recent decades.

Small Molecule Medicines Can Cross the Blood-Brain Barrier

Small molecule medicines are critical to reaching drug targets inside cells, but they also provide scientists with an essential tool to treat conditions that require overcoming one of the body's most important natural defenses: the blood-brain barrier.

The blood-brain barrier plays a critical protective role by regulating which substances can pass from the blood into the brain. This barrier is composed primarily of special brain cells that form a layer of tightly connected cell membranes separating the brain from circulating blood. The blood-brain barrier prevents damage to the central nervous system (CNS) by capitalizing on the physical barrier created by these "tight junctions" between cells as well as "transporter" proteins in cell membranes that control which substances can pass into and out of the brain. In addition to their protective functions, cells in the blood-brain barrier also interact with neurons and other brain cells to ensure that the CNS functions properly.[16,17]

Small molecule medicines targeting CNS diseases generally use one of three strategies to cross the blood-brain barrier: optimizing diffusion across the blood-brain barrier, using existing blood-brain barrier transporter mechanisms to carry medicines across or using targeted disruption of the blood-brain barrier that allows medicines to pass through. Small molecule medicines with particularly low molecular mass are able to cross the blood-brain barrier through passive diffusion, and this is the most common way that these medicines reach the brain.[18]

The blood-brain barrier, its transporters and related protective mechanisms are formidable barriers that inhibit delivery of medicines for diseases whose therapeutic targets are inside the brain. It is for this reason that the availability of medicines that are able to get past these barriers is critically important. This feature is also particularly valuable given that health conditions affecting the CNS and brain are common, including a range of mental illnesses, stroke, epilepsy, various neurodegenerative diseases such as Alzheimer's disease, dementia, Parkinson's disease and many more.

Case Studies Highlight the Importance of Small Molecule Medicines in Crossing the Blood-Brain Barrier

Although delivering small molecule medicines across the blood-brain barrier is extraordinarily challenging, the benefits of these medicines are clear for health conditions like depression, epilepsy, nerve pain and bipolar disorder. **The following examples demonstrate the critical importance of small molecule medicines for treating a wide range of health conditions impacting the CNS.**

- Selective serotonin reuptake inhibitors (SSRIs) are small molecule medications that work by increasing serotonin levels in the brain and are widely used for depression.[19] The prevalence and impact of depression are notable: in 2020, about 21 million adults experienced a major depressive episode,[20] and the high prevalence of this condition is linked to many unfavorable outcomes ranging from lower productivity at work to increased suicide risk.[21,22] Depression is also the most common mental illness affecting older adults.[23] Due to the mechanism of action of this class of small molecule medicines, SSRIs are also used to treat a range of other psychiatric conditions, such as anxiety disorders and post-traumatic stress disorder. Given the alarming increase in mental illness in recent years,[24] the ability of small molecule medicines like SSRIs to cross the blood-brain barrier and effectively treat many of these health conditions is critical to ensuring availability of effective treatments for mental health challenges.

- Anticonvulsants are another class of small molecule medications that provide great benefits to patients impacting the CNS. For example, gabapentinoids work through mechanisms that change how nerves send messages to the brain, and these medicines can be used to treat post-herpetic neuralgia (pain in the skin among people who have had shingles) and diabetic nerve pain. Some gabapentinoids are also used to treat seizures, reflecting the importance of these medicines for treatment of multiple health conditions affecting the CNS. One in three Americans will develop shingles in their lifetime, with about a million cases diagnosed each year.[25] About one-third of the 37 million Americans with diabetes will develop painful diabetic neuropathy, and about 3.4 million Americans have epilepsy, a figure that corresponds to approximately 1.2% of the total U.S. population.[26,27]

- The ability of small molecule medications to cross the blood-brain barrier also has obvious implications for age-related neurodegenerative conditions like Alzheimer's disease and Parkinson's disease, as well as conditions like multiple sclerosis. These neurodegenerative diseases are only a few examples of CNS-related conditions for which additional R&D on small molecule medicines would offer enormous benefits to patients and their families. About 6.5 million Americans have Alzheimer's disease, including 1 in 9 people over the age of 65, and Parkinson's disease and multiple sclerosis each affect an additional 1 million people in the United States.[28,29,30] Although all treatment options must be explored, development of small molecule medicines that can cross the blood-brain barrier have the potential to yield immeasurable benefits for patients and families affected by Alzheimer's and many other neurodegenerative diseases.

Small Molecule Medicines Can Improve Adherence and Reduce Health Disparities by Providing Greater Flexibility and Convenience for Health Care Providers, Patients and their Caregivers

Small molecule medicines offer important advantages which make them critically important for the health and well-being of all Americans. Not only can small molecule medicines be made in a wide range of dosage forms to meet a variety of patient needs, but they often can be easily stored in the home, reducing the need to administer medicines in a health care setting. These features in turn reduce barriers for patients to access and adhere to prescribed treatments, keeping patients healthy and reducing the need for use of other costly forms of medical care, while also reducing factors that drive health disparities.

Small Molecule Medicines Can Be Produced in Many Dosage Forms, Providing Greater Flexibility to Meet a Wide Range of Patient Needs

Small molecule medicines are most commonly available as pills, tablets or capsules, making them relatively easy to self-administer and often the preferred method by which to take a medicine. However, small molecule medicines can be formulated for administration in a wide array of dosage forms to meet the needs of diverse patient populations. A dosage form is the physical form a medicine takes to deliver an effective dose of the medicine's active ingredient to the patient. The FDA recognizes more than 150 dosage forms, including many types of tablets, syrups, solutions, granules, capsules, aerosols and injections.[31] Some examples of the flexibility and benefits of small molecule dosage forms include:

- **Coated tablets**: Protect medicines from degradation to extend shelf life
- **Flavored syrups**: Mask a medicine's bitter or salty taste for use by children
- **Suspensions**: Allow proper dosage of insoluble medicines for patients who cannot swallow pills
- **Powders for reconstitution**: Enable storage of medicine in a more stable form and extend shelf life before preparation in liquid form for patients who cannot swallow pills
- **Eye drops**: Provide sterile and particulate-free liquid dosage forms to prevent infection from administration
- **Intravenous (IV)**: For fast-acting treatment and to facilitate administration of higher doses
- **Injections**: Allow for targeted administration, including extended-release formulations that reduce barriers to following prescribed treatment protocols
- **Topicals or inhalants/aerosols**: Allow for targeted administration so the medicine can begin working quickly and reduce impacts on the rest of the body[32]

The availability of multiple dosage forms for small molecule medicines provides health care professionals with an array of options for treating different patient populations, age groups and conditions. Consider antibiotics, which are important tools for the treatment of various bacterial infections. For skin infections, antibiotics can be administered locally as creams, lotions, drops or sprays, and they can be given by injection for serious infections. For a bacterial ear or sinus infection, many patients can take antibiotics by mouth as tablets or capsules. However, for children who have not learned to swallow these oral dosage forms, antibiotics can also be administered as flavored oral suspensions.

Similarly, the wide availability of different dosage forms for small molecule medicines provides unique advantages for specific populations who have injection anxiety or are incapable of self-administering injections. For example, many children are afraid of needles, which can serve as a significant barrier to regular administration of medication.[33] Thus, the availability of different oral dosage forms in pediatric populations is critical. Likewise, in elderly and disabled populations, dosage forms that do not require self-injection or complicated instructions in order to administer correctly can be an important treatment option. Physical barriers like limited dexterity, lack of confidence in administering the injection and limitations in health literacy that inhibit self-injection are particular challenges in these populations.[34,35]

Conversely, in some treatment populations, the need to take a pill daily may prove particularly burdensome.[36] In these instances, the ability for small molecule medicines to be made available in multiple dosage forms often gives patients and health care professionals the choice to achieve treatment goals in a manner which provides them the greatest convenience and flexibility. For example, small molecule prophylactic medicines for HIV prevention are available not only in a once-daily pill but also as a long-acting injectable administered by a health care professional once every few months.[37] Similarly, small molecule antipsychotic medications for the treatment of schizophrenia are available in both daily oral dosage forms as well as long-acting injectable formulations, enabling patients to receive an injection from a health care professional every few weeks or months. The key feature of long-acting options is the ability to reduce variability in self-administered dosing, helping to maintain more consistent levels of medicine sustained over a period of time. These features in turn are associated with a reduction in relapses and associated hospitalizations and health care costs.[38,39,40]

The ability to adapt and respond to differences in care delivery outside of the hospital setting (outpatient) vs. a hospital inpatient setting is another example of the value of having small molecule medicines available in different dosage forms. In the outpatient setting, patients are often able to take medications by mouth, but in many cases, critically ill hospitalized patients and those in emergency rooms are too sick to swallow needed medicines and are given these treatments by injection or intravenously.

Small Molecule Medicines Provide Significant Convenience for Patients

The most convenient medicine to self-administer is often the one in your home, which can be stored there for relatively long periods of time and is available with minimal visits to the pharmacy, doctor's office or infusion center.

Most Small Molecule Medicines Can Be Stored Relatively Easily at Home

It is important that all medicines are stored correctly to prevent degradation and loss of effectiveness, and recommended storage conditions vary for each medicine and dosage form. For example, many medicines need to be stored at certain temperatures, while others are sensitive to light and fluctuations in temperature and humidity.[41] However, most small molecule medicines that are taken as oral dosage forms like tablets and capsules are relatively easy to store at home, for example in the medicine cabinet, because their integrity can be maintained at room temperature, and they have a relatively long shelf life. These characteristics greatly enhance the convenience offered by many of these medicines, thereby reducing barriers to patients taking medicines as prescribed.

Due to their long shelf life, storing small molecule oral dosage forms in the home can also translate to fewer visits to the pharmacy, which is particularly valuable for helping elderly and disabled populations as well as those with socioeconomic challenges. Because small molecule medicines are shelf-stable, many community and mail-order pharmacies allow patients to access 90-day supplies of many medicines. This reduces the number of trips patients must make to the pharmacy to drop off and pick up their prescriptions. The increased convenience associated with saved trips is especially helpful to patients who take multiple medications, those who must travel long distances to reach a pharmacy, people without access to transportation, and those with physical limitations that create challenges for pharmacy access.

To put the burden of frequent pharmacy visits into context:

- There are approximately 56 million people in the United States over the age of 65. Of these, 89% take at least one prescription medication, and 54% take four or more medicines.[42,43] This translates to more than 1.4 billion trips to the pharmacy each year for patients taking four or more medicines.[44]
- For older adults with physical challenges, these trips can create barriers to accessing needed medicines. And the share of older adults with these challenges is substantial: 41% of adults aged 65 to 79 have at least one limitation in self-care, mobility or taking care of their households, and this rises to 71% among people 80 and older.[45]

Small Molecule Medicines Decrease the Need for Administration of Medicines in a Health Care Setting

There are many important reasons why some medicines need to be administered in a health care setting. These include requirements for a health care professional to administer and monitor the short-term side effects of a medicine or the need for the medicine to be specially handled or stored according to specific standards that cannot be maintained in a person's home. For patients with cancer, multiple sclerosis and various autoimmune disorders such as rheumatoid arthritis or Crohn's disease, for example, the most effective treatment option for some patients may require regular infusions with biologic medicines at an infusion center which may take several hours to administer a medicine.[46] But for patients with health conditions that can be effectively treated with small molecule medicines, the ability to administer a medicine at home eliminates many of the challenges associated with repeated trips to the doctor's office or infusion center for treatment.

Despite the requirement that some medications be administered in a health care setting, it is important to acknowledge that the need to travel regularly to a doctor's office to receive medication introduces formidable challenges for some patients. Social needs like housing and food insecurity, health-related travel costs, lack of personal transportation or access to adequate public transportation and the need to secure care for children or aging parents are all factors that create challenges for patients to maintain a regular schedule of doctor appointments. As the number of social needs increases, so too does the likelihood of not keeping needed appointments.[47] For some patients, taking time off from work to see their doctor results in a meaningful loss of income. For others–especially low-income women–problems securing and paying for safe childcare is the most common reason for not seeing their doctors.[48] These challenges are particularly compounded among patients who need to receive a physician-administered medicine in an office setting or infusion center.

> ***"There's a lot of people who live in poverty who don't have family or reliable transportation who can't afford the two dollars they charge you to take one way on the bus."***
>
> ***–Patient in study of low-income individuals who missed doctor's appointments***

People who live in rural areas face extraordinary challenges accessing health care and these challenges are especially pronounced for specialty care.[49,50] Approximately 46 million Americans–14% of the total population–live in rural areas,[51] underscoring the impact of geography on treatment access. But because small molecule medicines can most often be self-administered in the home as opposed to administered in a doctor's office or infusion center, they can greatly help to address this challenge.

Small Molecule Medicines Reduce Barriers to Medication Adherence

Flexibility and convenience are invaluable characteristics of small molecule medicines. Dosage form is an important driver of medication adherence, and the availability of small molecule medicines in a wide range of dosage forms provides important benefits for helping patients remain adherent to their prescribed treatment regimens.[52,53] This can be especially true for those who are chronically ill, people with disabilities and older adults, as they tend to take more medications. It is also true because disease progression and age-related changes such as reduced cognition, vision and motor function can impact the ability of these populations to remain adherent to their treatment regimens.[54]

A large body of evidence demonstrates that better use of medicines and medication adherence can prevent disease progression and reduce the use of costly hospital and emergency care across a broad range of chronic conditions, especially in the Medicare population.[55,56] For example, as a result of seniors and people with disabilities gaining Medicare Part D prescription drug coverage–which covers primarily small molecule medicines–Medicare saved $27 billion due to improved adherence to congestive heart failure medications alone.[57] Other research shows that improving adherence for common chronic conditions like diabetes, high blood pressure and high cholesterol could each save the Medicare program between $4.5 billion and $13.7 billion annually, primarily from fewer inpatient hospital stays and avoidable emergency department visits.[58] The characteristics of small molecule medicines, in that they offer great flexibility and convenience to patients, therefore not only reduce many of the factors that drive non-adherence but also the significant health care costs that are associated with patients not taking medicines as described.

Small Molecule Medicines Can Reduce Barriers to Health Equity

Unfortunately for many Americans, the barriers that stand in the way of better health are not simply a matter of convenience but reflect broader and more pervasive limitations. Social determinants of health are the conditions in the environments where people are born, live, learn, work, play, worship and age that affect a wide range of health functioning and quality of life outcomes and risks.[59] These factors contribute to wide health disparities and inequities. For example, in the United States, 1 in 10 people live in poverty and many people can't afford transportation, many have trouble finding or keeping a job, or struggle to afford care for a child or parent.[60] Housing instability, unemployment and inadequate social support are just some of the social determinants associated with poor adherence to medicines.[61] These factors have a disproportionate impact on disadvantaged patients who are least positioned to handle them–including, in particular, elderly and disabled patients who often have multiple chronic conditions.

The relative convenience offered by small molecule medicines–which may be stored safely at home in one's medicine cabinet, necessitating fewer trips to the pharmacy or visits to a doctor or an infusion center–can help reduce the burden of transportation limitations and the caregiver costs, lost wages and other hurdles that have played a role in driving longstanding health inequities. For this reason, small molecule medicines can have particularly beneficial impacts for underserved or disadvantaged patients, many of whom face additional barriers to accessing care and are disproportionately burdened with poor health outcomes. By offering a more convenient option for patients, small molecule medicines can help to overcome some of the social barriers to adhering to prescribed medicines and offer an opportunity to achieve better health outcomes regardless of socioeconomic status.

Conclusion

Both small molecule and biologic medicines serve unique purposes in treating a wide range of diseases impacting patients in different and distinct ways. Due to their unique clinical characteristics, however, small molecule medicines provide essential treatments for a wide range of health conditions that are common among older, disabled and chronically ill populations–including cancer, psychiatric conditions, central nervous system illnesses and many more. This is in part because small molecule medicines have the ability to target medicines inside cells and cross the blood-brain barrier. Small molecules also provide great flexibility, reducing barriers to adherence which can exacerbate health disparities.

Unfortunately, the timeline established under the Inflation Reduction Act for setting prices of small molecule medicines undermines the incentives to invest in these treatments, ignoring many of these indispensable attributes that have made them particularly valuable to patients and our health care system. To continue to incentivize their development, policymakers should change the timeline for price setting these medicines such that they may not be selected for price setting until 11 years following FDA approval, and the government-set price should not go into effect until 13 years following FDA approval. These changes can have a meaningful impact on the R&D decisions that biopharmaceutical companies are having to make now and help ensure patients can continue to realize the benefits these medicines have to offer, now and into the future.

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