



Value and Innovation

2019 Report

This report is intended for U.S. government officials, other healthcare policy makers and healthcare policy opinion leaders



Betty Merker was diagnosed with multiple myeloma

Letter from Chairman and CEO Mark Alles

To Our Stakeholders:

“Value” and “innovation” may be two of the most important words in healthcare.

As the debate about healthcare costs intensifies, this report has been generated to describe how Celgene defines value and innovation, and how we – and others – can measure our progress as a company and as a partner working to improve human health.

To a patient, value can mean extended survival or days without pain. To a hospital manager, value can mean more patients going home healthy and at lower risk for future readmission. To society and the economy, value can mean fewer people requiring complex medical care, increased productivity due to reduced sick days, and a healthier population. And to future innovation, value means an environment that incentivizes disease-changing scientific research and life-changing clinical development.

No other sector of the economy touches people and society as broadly as healthcare, which is why any assessment of healthcare costs, and the associated value, must be holistic and multi-dimensional. Since last year’s report, we have continued to see measurable improvements in outcomes associated with innovative therapies. These improvements frequently result in reduced costs for in-hospital or other forms of healthcare.

Value lies at the intersection of costs and benefits; viewing one without considering the other risks potentially short-sighted decisions that undervalue innovative therapies that doctors and patients so badly need.

Yet healthcare costs are an important concern. Celgene continues to adhere to our Principles for the Pricing of Innovative Medicines, and we are working collaboratively with governments, health systems, payors and other stakeholders to find constructive solutions to issues of cost and access. In 2018 and 2019, we have limited price increases for our products to no more than once per year and at a level no greater than medical inflation (CMS projected growth rate for National Health Expenditures for the year), to provide predictability for payors and patients alike.

We believe in the virtuous cycle of innovation: the idea that the success of today’s treatments allows us to invest in tomorrow’s breakthroughs. That’s why, of all the numbers we use to define and assess value, none is more important than 39 – the average percentage of revenues that we have directed back into research and development (R&D) over the last five years, more than any other major biopharmaceutical company and among the very highest of any large company anywhere in the world. To be sure, that is not the only benchmark by which we measure our progress, but it best demonstrates how my more than 8,500 Celgene colleagues around the world work to define value: delivering on the promise our therapies have for patients today and researching future innovation for the patients of tomorrow.



Mark J. Alles, Chairman and Chief Executive Officer



About This Report

The Celgene Value and Innovation Report is a yearly assessment of the different ways in which Celgene's pursuit of innovation creates value for patients, the health system, the economy and society, and future innovation. This report has been developed to contribute to the U.S. healthcare policy discussion. Therefore, it is intended for U.S. government officials, other healthcare policy makers and healthcare policy opinion leaders. Celgene issues this report on an annual basis to track its progress using the value framework laid out within.

The Value and Innovation Report can be accessed online at:
<http://www.celgene.com/value>

Annual reports and other financial information for Celgene are available at:
<https://ir.celgene.com/investors/default.aspx>

More information on the company's commitment to being a responsible corporate citizen can be found at:
<http://www.celgene.com/responsibility/>

This report is intended for U.S. government officials, other healthcare policy makers and healthcare policy opinion leaders.



Celgene Product Information

This report includes information related to the following Celgene therapies:



For prescribing information for REVLIMID[®],
including Boxed WARNINGS, please visit:
<http://media.celgene.com/content/uploads/revlimid-pi.pdf>

REVLIMID[®] is a registered trademark of Celgene Corporation.



For prescribing information for OTEZLA[®], please visit:
<http://media.celgene.com/content/uploads/otezla-pi.pdf>

OTEZLA[®] is a registered trademark of Celgene Corporation.



For prescribing information for POMALYST[®],
including Boxed WARNINGS, please visit:
<http://media.celgene.com/content/uploads/pomalyst-pi.pdf>

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For prescribing information for IDHIFA[®],
including Boxed WARNINGS, please visit:
<http://media.celgene.com/content/uploads/idhifa-pi.pdf>

IDHIFA[®] is a registered trademark of Celgene Corporation.



For prescribing information for ABRAXANE[®],
including Boxed WARNINGS, please visit:
<http://media.celgene.com/content/uploads/abraxane-pi.pdf>

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Susan Freeman
was diagnosed with
plaque psoriasis

Celgene Approach to Value

Continuing the Commitment

“The pricing of innovative medicines is complex but ultimately must strike a balance between ensuring access for every patient who may benefit and preserving incentives for medical innovation and investment in research and development. If we meet these goals, we can continue to deliver life-changing treatments today, invent tomorrow’s breakthroughs, and fuel a sustainable, virtuous cycle of innovation.”

– Celgene Principles for the Pricing of
Innovative Medicines

In the year since Celgene released its first Value and Innovation Report, there have been continued efforts across the healthcare sector to address both overall healthcare costs and prescription drug spending. At the same time, the drive to expand access to quality care remains a priority in the United States and around the world. While specific circumstances vary from region to region, the challenge to align healthcare costs with value is a common goal for governments and health systems around the world.

Recent data indicates progress is being made at achieving more of that balance in the United States. In 2017, prescription drug spending on a per capita basis went down slightly (0.3 percent), the first decline since 2012.¹ Overall, healthcare inflation also stabilized. Instead of 12 percent annual growth that was typical in the 1970s, healthcare costs have grown since 2010 at an average of 3.6 percent, close to the overall inflation rate (3.1 percent).²

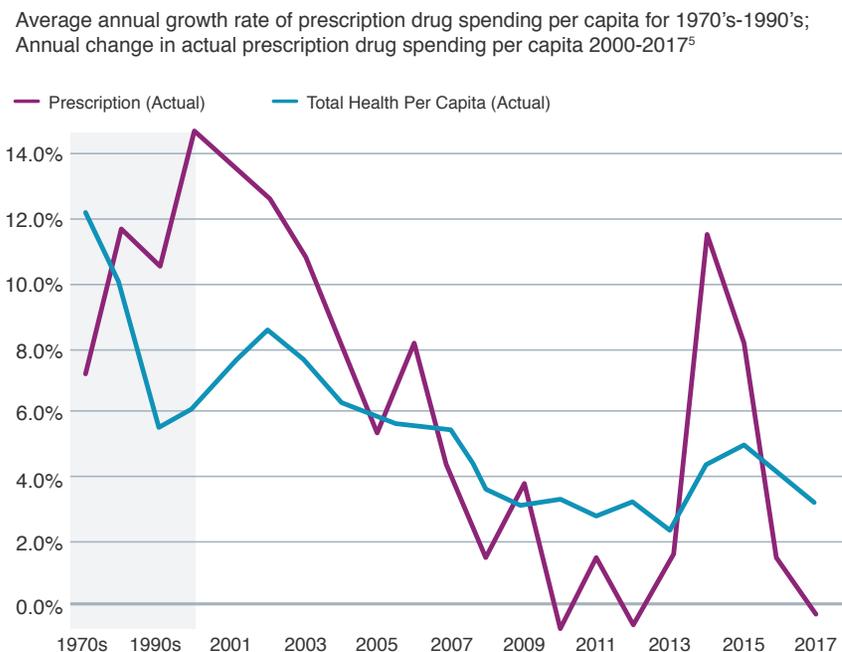
In 2017, total prescription drug spending in the United States increased 0.4 percent, much lower than the 2.6 percent increase in 2016 – and less than spending on physician and clinical services, which increased by 4.2 percent in 2017.³ However, the latest National Health Expenditures projection from U.S. Centers for Medicare & Medicaid Services (CMS) estimates that total prescription drug spending went up 3.3 percent in 2018 and will grow an average of 6.1 percent per year from 2020 to 2027.³ The CMS estimate attributes this growth to a combination of new drugs becoming available and increased efforts to get patients to take medicines as prescribed.⁴

For its part, Celgene’s commitment to holistic transparency throughout the healthcare system is stronger than ever. When policy makers, consumers, investors and other stakeholders has access to more complete information about healthcare spending and the myriad factors involved in healthcare costs, they are better able to properly evaluate the value received.

The 2019 report looks at how Celgene and other biopharmaceutical companies collectively deliver on value and innovation and adds meaningful data to the ongoing effort to improve healthcare and expand access.

While recent uncertainty in the healthcare policy environment has added challenges for every stakeholder, the determination to discover and develop drugs that address important healthcare needs has not wavered. Breakthrough medicines that result from collaborations with partner companies and academic institutions, as well as Celgene’s own R&D, make a difference for patients around the world.

The average annual growth rate of prescription drug spending per capita in the U.S. has been declining since 2014



Gray region represents average growth within decade.

Source: Kaiser Family Foundation analysis of National Health Expenditure (NHE) Historical (1970-2017) data from Centers for Medicare & Medicaid Services, Office of the Actuary, National Health Statistics Group (Accessed on December 6, 2018)

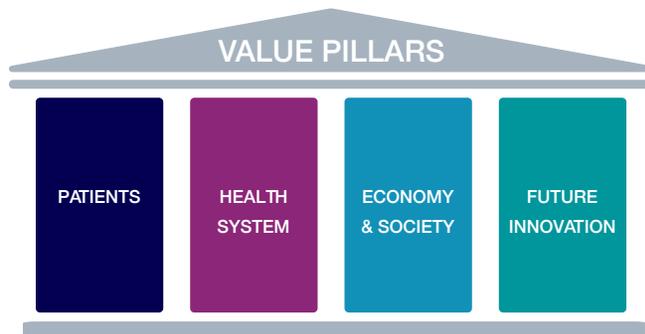


Value means different things to different people, so any measure of value must examine different perspectives. This report provides a framework for informed discussion among stakeholders in different positions but who all want the benefits of modern medicine and share in the commitment to provide access to quality healthcare and improve patient outcomes.

In our 2018 report, we outlined the four pillars that constitute value, taking into consideration the stakeholders engaged in healthcare innovation and delivery:

- Value to patients
- Value to the health system
- Value to the economy and society
- Value to future innovation

These four pillars provide a lens through which healthcare costs can be viewed and evaluated. We believe this approach allows an informed comparison across different therapies, including hospitalizations and other interventions – not just prescription medicines. By addressing all four pillars, Celgene strives to fulfill its purpose of changing the course of human health through bold pursuits in science, with a promise to put patients first.



For more information on how Celgene delivers on value, innovation and transparency, please visit the Celgene Value Hub at www.celgene.com/Value.



By the Numbers

Celgene has the highest R&D intensity (defined as the ratio of R&D spending to net sales) among biopharmaceutical companies and ranks **No. 3 globally** among companies in all industrial sectors, according to the European Commission. Four of the top 10 most R&D-intense companies in the world are biopharmaceutical firms⁶

39%

Average percentage of revenue reinvested by Celgene in R&D over the past 5 years^{7*}

* Numbers based on Generally Accepted Accounting Principles

\$22 billion

Committed to R&D by Celgene between 2014 and 2018^{7*}

* Numbers based on Generally Accepted Accounting Principles

In 2016, biopharmaceutical companies spent some **\$159 billion dollars** on R&D. Based on historical year-to-year growth, this will grow to over **\$200 billion dollars** in 2024⁸

~ 7,000

Medicines in clinical development across the biopharmaceutical industry⁹

74%

Percentage of drugs in clinical development across the biopharmaceutical industry that have the potential to represent new and unique mechanisms of actions⁹

1,900

Drugs in development across the biopharmaceutical industry for cancer¹⁰

Hannah Maldonado
was diagnosed with
multiple sclerosis



Value to Patients

“Celgene is focused on the discovery, development and commercialization of innovative therapies for unmet medical needs in cancer and immune-inflammatory diseases.”

– Celgene Mission Statement

Value to Patients

Everything Celgene does advances the discovery and development of innovative medicines that improve people's lives. Our focus is, and always has been, improving health outcomes and extending survival.

We are proud that our therapies have helped patients realize dramatic improvements in diseases such as cancer and inflammatory conditions. People are living longer, healthier lives than ever before, and much of the increase can be attributed to innovative medicines. In fact, one study that looked at 30 developing and developed countries between 2000 and 2009 found that access to new therapies accounted for 73 percent of the increase in life expectancy.¹¹

Value to patients has many dimensions. Celgene believes that measurable value comes from:

- Improvement in patient outcomes
- Improvements in quality of life
- Provision of patient education and support

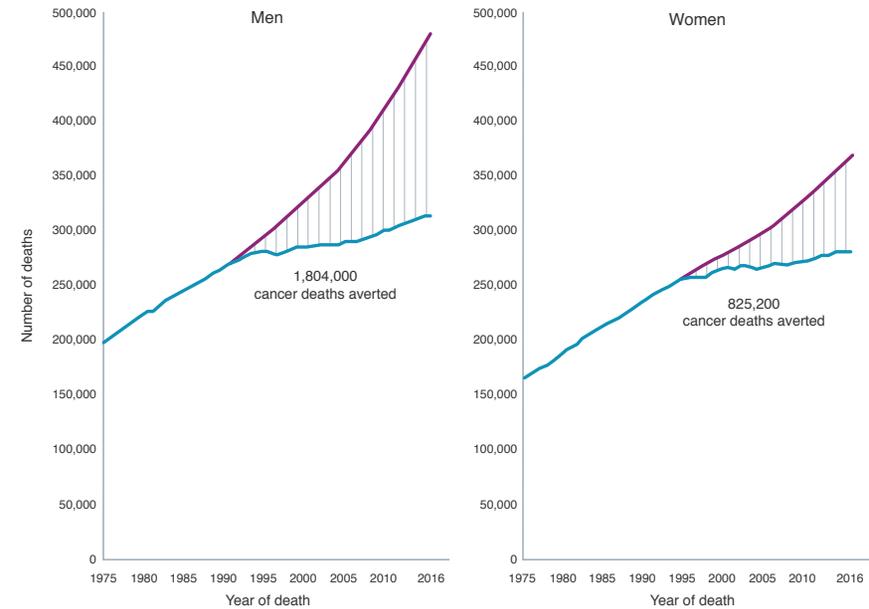
However, value is much more than these metrics. For adults and children diagnosed with cancer, breakthrough medicines introduced within the past few years are not only extending survival but also bringing us closer to a day when their disease can be managed as a chronic disease, and hopefully ultimately cured.

While the goal of eliminating cancer as a cause of death remains elusive, new drugs may give patients precious time and potentially better quality of life in which to spend that time. Empowering patients to live longer and fuller lives means they can be present for family events, spend time with loved ones, and have more control over how they live their lives.

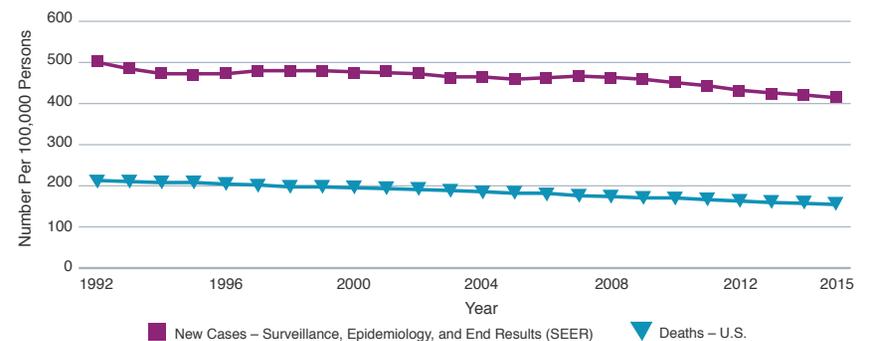
Reducing the burden of disease and increasing productive time are among the most important kinds of value that innovative medicines deliver to patients. From 1995 to 2015, survival increased for people with lung cancer, heart disease and HIV/AIDS, while the cost of care for these diseases went down (when adjusted for inflation). This is a result of a combination of medical advances, availability of lower cost generic drugs, and the economic benefits accrued when people are healthy instead of sick.¹²

The pace of innovation has also picked up – dramatically – with tangible benefits to patients every day. From 2009 to 2017, an average of 33 new drugs was approved each year by the U.S. Food and Drug Administration (FDA), but, in 2018 alone, the FDA approved 59 new drugs.¹³ In the field of cancer therapies, the innovation rate has been especially fast. More than 63 new cancer drugs were launched between 2012 and 2017,¹⁷

New therapies contribute to an increase in the number of cancer deaths averted
Blue line represents actual U.S. deaths; purple line represents the number of deaths that would have been expected in the U.S. if cancer death rates had not declined¹⁴

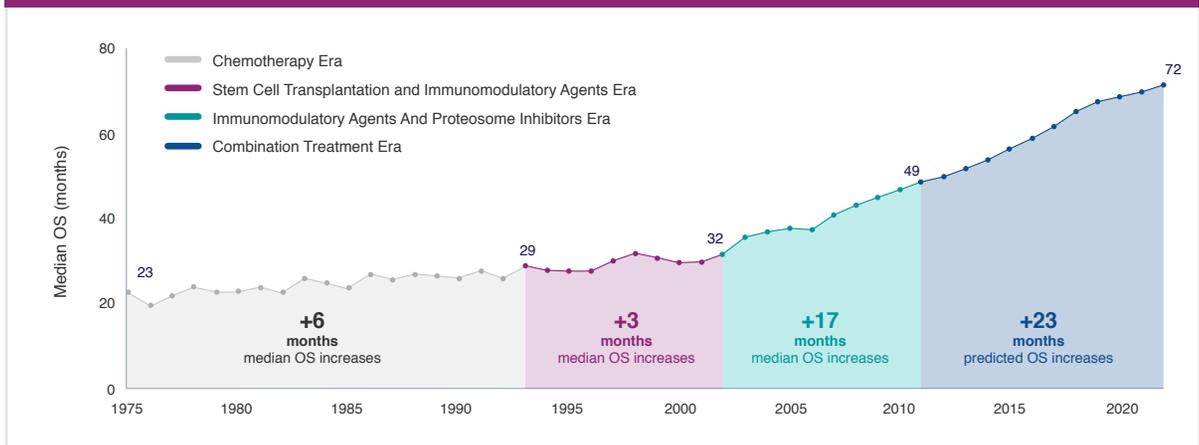


Overall cancer death rate in the U.S. decreased 27% from 1991 to 2016
Decrease resulted in 2,629,200 fewer cancer deaths¹⁵



Innovation contributes to overall survival (OS) gains in the U.S. for patients with multiple myeloma

Advances in multiple myeloma treatments continue to improve relative survival rates for patients¹⁶



and, in 2018 alone, the FDA approved another 18.¹³

The progress extends well beyond cancer, however. Among new drugs approved in 2018, 34 treat rare diseases and 14 were considered “breakthrough” medicines because they work for patients whose other treatment options have been limited.¹³

While some medicines have high costs, patient outcomes are improving, including in some of the hardest to treat diseases. The newest cancer medicines are targeted therapies with clinically significant results, such as limiting cancer growth, reducing tumor size, or extending overall survival (OS).¹⁷

The development of innovative new medicines and a greater understanding of diseases and their effects on patients gives people control over their own healthcare in ways that were not possible before. Knowledge of diseases, the human body and how they respond to treatment has inherent value – and contributes to improved outcomes by helping people understand their health and their medicines. In turn, this helps control overall treatment costs.

For example, among patients with multiple sclerosis (MS), those who use their prescription medicines as directed

can reduce their relapse rate and risk for hospitalization.¹⁹ Recent research found that 80 percent of avoidable healthcare expenses among MS patients may result from patients not taking their medicine as prescribed.²⁰

Of course, there are many factors that contribute to patients not using medicines as directed. In addition to misunderstanding prescriptions, many people struggle to pay the out-of-pocket drug costs required by health insurers. Employees with health insurance through their work paid 54 percent more out of pocket toward medical expenses in 2016 than in 2006.²¹

Adding to the problem is the large difference between out-of-pocket costs for drugs obtained from a local pharmacy and treatments administered at a hospital or clinic. Insurers sometimes charge patients amounts up to thousands of dollars out of pocket for medicines dispensed at pharmacies, while the co-pay for an intravenous cancer treatment given in a clinic is typically considerably lower. More than 91 million Americans remain exposed to this flaw in their health insurance plans.²²

For these reasons, Celgene supports legislation at the state and federal levels that would require insurers to cover oral cancer drugs on the same cost-sharing basis as intravenous cancer treatments, a proposal known as oral parity. Patients



James Castro was diagnosed with multiple myeloma



cannot receive the value possible from the most innovative medicines if they cannot afford the medicines in the first place.

By focusing on value to patients, Celgene develops life-changing therapies for difficult-to-treat conditions, even when only a small number of patients may be eligible for the treatment. One example is IDHIFA® (enasidenib), which was approved by the FDA in 2017 for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) who have a specific genetic mutation.²⁴ There were an estimated 19,520 new cases of AML diagnosed in the United States in 2018.²⁵

This targeted therapy has a significant, measurable impact on a narrow population – about 10 percent of

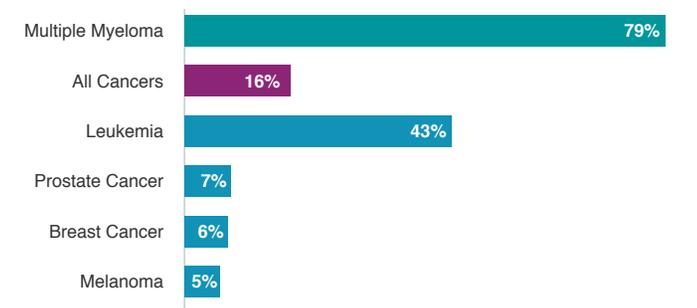
independent, during any 56-day post baseline assessment during the study, reducing one of the major burdens for AML patients.²⁸

Another Celgene drug, OTEZLA® (apremilast), has been proven to make a big difference in the everyday lives of appropriate patients with the condition of moderate to severe plaque psoriasis. Plaque psoriasis is a multi-faceted disease that can manifest in numerous ways. Each patient has a different experience, and many are concerned about effects that go beyond the skin. This need for patient-centric care has been recognized by the World Health Organization, and represents a shift in the focus from treating the skin lesions of psoriasis to addressing the needs of the whole patient.³⁰

Improving the quality of life for people living with chronic conditions provides important value to those patients and their families.

Relative survival rates for multiple myeloma are increasing more quickly than all cancers

Relative 5-year survival rates for multiple myeloma increased more than four times faster than for all cancers in the U.S. (1990-2014)²³



AML patients have the specific mutation,²⁶ and about half of those patients are potential candidates for treatment with IDHIFA because they have relapsed after prior treatment.²⁷

Patients with relapsed or refractory AML have a very poor prognosis, typically surviving less than four months. In clinical studies, about one of every five people treated with IDHIFA had a complete response with a median duration of 8.2 months, and one out of three became transfusion

Value in Action: How Innovative Contracting Can Reduce Patients' Costs

In an effort to ensure that patients who would benefit from IDHIFA have access to it, Celgene pursued an innovative contracting approach to access and reimbursement with some of the leading payor groups in the United States.

For commercial patients insured by participating payor groups, the Celgene approach eliminates their financial liability for this medicine. As long as patients have no co-pay obligation, Celgene will pay a rebate to insurers for every IDHIFA prescription.

Celgene developed this program specifically for IDHIFA-eligible patients who were unable to meet the eligibility requirements for Celgene Patient Support® yet still required additional assistance. The IDHIFA contract also extends coverage beyond when patients meet their out-of-pocket maximum, resulting in savings not just to the patient but to the entire healthcare system.

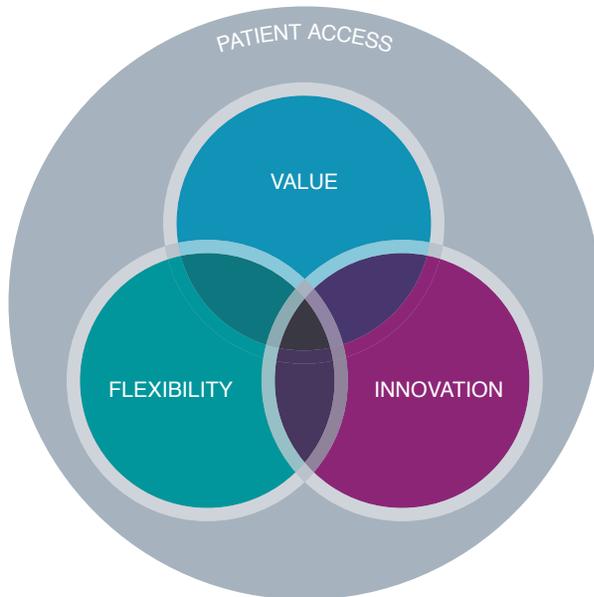


At Celgene, we adhere to our Principles for the Pricing of Innovative Medicines, which guide how we get our innovative therapies to the patients who can benefit from them. We work collaboratively with governments, health systems, payors and all other stakeholders to find constructive solutions to pricing and access issues. By limiting price increases to once per year and at a level no greater than medical inflation (CMS projected growth rate for National Health Expenditures for the year), we provide predictability for payors and patients alike.

And because value is a guiding principle of our pricing decisions, there may be exceptional circumstances in which additional clinical or health economic evidence demonstrates a clear and significant increase in the value of one of our medicines where this standard would not apply.

We aspire to provide every patient with the medicine they need, but this requires the collaboration of all stakeholders. Patient access is a shared goal – it cannot be achieved by biopharmaceutical companies alone.

Celgene Principles for the Pricing of Innovative Medicines



Judith Harding was diagnosed with multiple myeloma

Celgene Patient Support® Program

For individuals who have questions or need help understanding how to access their medicines, Celgene Patient Support® helps patients navigate available insurance or other benefit programs. Some patients may qualify for assistance that brings their co-pay responsibility to \$25 or less. And for OTEZLA in particular, patients with private insurance can pay \$0 through the OTEZLA SupportPlus™ program.

Patients can access the Celgene Patient Support® Program at: <https://www.celgenepatientsupport.com/>

Patients taking OTEZLA can access the OTEZLA SupportPlus™ program at: <https://www.otezla.com/supportplus>



By the Numbers

Value to Patients

500,000+

Patients prescribed Celgene products globally in 2018³¹

250

Partnerships with patient groups around the world³²

102,000+

Patients who received support and education from Celgene in 2018³³

360,000+

Patients who have received support and education from Celgene to date³²

To deliver on our promise of putting patients first, Celgene provides substantial support to patients who have trouble accessing their medicines through our Patient Assistance Program and the Celgene Commercial Co-pay Program.

— IN 2018, OVER —
20,000 PATIENTS
ACROSS 8 DIFFERENT MEDICINES,
WERE SUPPORTED BY THE CELGENE
PATIENT ASSISTANCE PROGRAM

— OVER THE PAST THREE YEARS, —
THE CELGENE PATIENT ASSISTANCE PROGRAM
HAS PROVIDED PATIENTS WITH ABOUT
\$2B OF FREE MEDICATIONS 

— OVER THE PAST THREE YEARS, —
139,000+ PATIENTS
WITH COMMERCIAL INSURANCE
HAVE RECEIVED CO-PAY SUPPORT
FROM CELGENE 

— BETWEEN 2016–2018, —
CELGENE CO-PAY SUPPORT
RESULTED IN OVER
\$304M IN SAVINGS
TO PATIENTS WITH
COMMERCIAL INSURANCE



Value to the Health System

“The need to invest in medical innovation has never been more important as the population ages, the burden of disease increases, and scientific advances allow better targeting of disease.”

– Celgene Principles for the Pricing of Innovative Medicines

Value to the Health System

Celgene's goal is to contribute to a healthcare system that promotes good health and incentivizes innovation. Medicines are only one element in the interconnected web that is today's healthcare system. While prices paid for innovative medicines incentivize companies like Celgene to continue developing novel therapeutics to treat or prevent disease, value to the healthcare system goes well beyond new drugs.

Innovative medicines deliver value to the healthcare system in ways beyond improved patient outcomes. At Celgene, we define the value we provide to the healthcare system as:

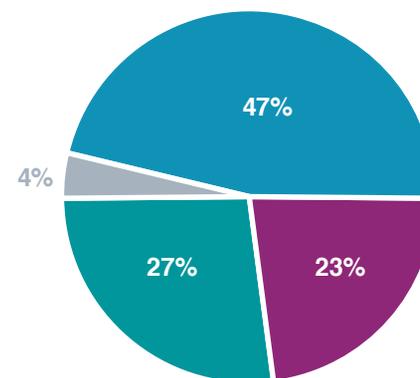
- Cost savings when better therapies reduce the need for other medical services, like hospital stays
- Investment in academic research, investigator-initiated clinical trials, and real-world evidence
- Support for physician education and other healthcare system capacity building

Even accounting for high-priced innovative therapeutics, prescription costs are only part of the healthcare system and one of many drivers of healthcare costs. Total spending on prescription medicines in the United States – both retail and inpatient – constitutes about 16 percent of the total amount spent on healthcare.³⁴ For people covered by private insurance, the range is 17 to 21 percent of total spending.³⁴

According to CMS, overall healthcare spending is increasing by nearly 4 percent a year. Hospital care, which makes up 33 percent of healthcare spending, grew 4.6 percent in 2017 and physician and clinical services, 20 percent of the healthcare pie, was up 4.2 percent.³⁴ Meanwhile, CMS found that spending on retail prescription drugs grew by only 0.4 percent in 2017.³⁴

In Europe, pharmaceutical spending accounts for between 11.4 and 19.1 percent of total healthcare expenditures across the largest five European markets – France, Germany, Italy, Spain and the UK.³⁵ However, there are signs of an increasing divergence between net and list price in these markets which may indicate pharmaceutical spending increases are lower than previously reported.³⁶ Taken in aggregate, historic price increases (2010-2016) fell from 3.4 percent at list to 2.5 percent at net, and projected increases decreased from 2.9 percent at list to 1.5 percent at net, a number that is in line with long-term projected growth rates.³⁶

U.S. brand manufacturers realized less than half of net spending on prescription drugs in 2015³⁷



* Includes any retrospective rebates and fees not shared with the end payor

■ Brand Manufacturers ■ Generic Manufacturers ■ Supply Chain Entities ■ Other Retrospective Rebates and Fees

MANUFACTURERS	Net Expenditures	
	\$ (Billions)	%
Brand Manufacturers	\$218.6	47%
Generic Manufacturers	\$107.6	23%
NON-MANUFACTURER STAKEHOLDERS		
Supply Chain Entities	\$125.3	27%
Other Retrospective Rebates and Fees*	\$17.5	4%
Total†	\$469.0	100%

† Components may not sum to total due to rounding



To answer the question of what value is received for the money spent on innovative drugs, one must look at overall costs, both the hard costs of medical services and the reduction in disease burden overall. One study that looked at major diseases – lung cancer, heart disease, HIV/AIDS, breast cancer, diabetes and chronic obstructive pulmonary disease (COPD) – found that between 1996 and 2015 increased spending to treat the disease reduced overall healthcare costs in all of these conditions except COPD.¹² Additionally, per person costs for four of the conditions decreased, while the remaining three increased modestly.¹²

Biopharmaceutical companies are among the most research-intensive businesses in the world, and Celgene reinvests a higher percentage of its revenues into R&D than any other biopharmaceutical company (on a Generally Accepted Accounting Principles basis).¹⁰ Our investment in academic research and collaborations with startups and other organizations promote new knowledge, including “real-world” data that informs clinicians and scientists about how medical interventions work beyond the boundaries of clinical studies.

Analyzing value at the system level provides the opportunity to address healthcare needs at the macro level, by focusing on outcomes, total costs, and overall impact instead of individual expenses. Also, because biopharmaceutical companies negotiate discounts and rebates with insurance companies and other healthcare payors, any analysis at the healthcare system level must distinguish between “list prices” and prices actually paid. Factoring in discounts and rebates, overall biopharmaceutical price increases in the United States are significantly lower than the 5.5 percent growth of list prices in 2017.³⁸ The average rebate to pharmacy benefit managers, insurance companies and other wholesale purchasers is estimated at more than 40 percent off list price.³⁸

While innovative medicines do initially generate revenue for the innovator, they ultimately go off patent, enabling society to benefit indefinitely from the availability of low-cost generic alternatives. Without the original R&D of the innovative medicine, generic alternatives would not exist. This is the lifecycle of biopharmaceutical products: As patent exclusivity for existing treatments expires, prices drop substantially, and innovators can only be successful by discovering and developing new, more effective treatments. The savings from new generic equivalents and “biosimilars” are substantial, and the FDA has sped up approval of generics.³⁹

The result balances overall spending, as new drugs may be costly but older drug prices drop as much as 80 percent once generic versions are available.^{39,40} In the United States, generics are dispensed in nine out of every 10 prescriptions.⁴¹ Furthermore, given that generics are typically priced substantially less than a patent medicine, generics saved over \$1 trillion in healthcare expenses from 2008 to 2017, including \$265 billion in savings for all generics and almost \$10 billion in savings for newly approved generics in 2017 alone.^{40, 42, 43} In addition to the resulting cost savings, generics represent a way to treat many more patients with effective treatments. This is especially critical in an aging society that is increasingly reliant on prescription medicines to manage chronic conditions such as high cholesterol, hypertension and diabetes.



Leika Pina-Santiago
was diagnosed with
multiple sclerosis

Increasing access to biosimilars has the potential to reduce healthcare costs in the United States by up to \$54 billion over 10 years.⁴⁴ The Center for Biosimilars reports that by 2020 biosimilars could save up to \$113 billion in Germany, France, Italy, Spain, the United Kingdom and the United States.⁴⁵

For medicines to be optimally effective, they have to be taken correctly.⁴⁶ While there are many factors that influence adherence, healthcare providers, including physicians, nurses and pharmacists, have a critical role to play in ensuring patients are adhering to their medication regimens.⁴⁷ As healthcare providers work together to implement programs aimed at improving adherence, savings may be realized in terms of preventable hospitalization and disease-specific medical costs.^{48,49} In order to make these programs the most effective, and for the biopharmaceutical industry to assist professionals in enabling adherence, there are regulatory barriers that will need to be eliminated, including restrictions on the information payors and manufacturers can share when contracting toward high-quality care, existing reimbursement mechanisms that may not cover adherence programs and laws governing how organizations can partner.⁵⁰

Competition from generics and biosimilars is expected to reduce U.S. brand sales by \$95 billion from 2019 to 2023⁵¹



Source: IQVIA Market Prognosis, Oct 2018; IQVIA Institute, Dec 2018
Report: The Global Use of Medicine in 2019 and Outlook to 2023, IQVIA Institute of Human Data Science, Jan 2019

■ Small Molecules ■ Biologics ■ Health System Savings Due to Losses of Exclusivity

Value in Action: Using a Crowdsourced Approach to Improve Patient Stratification in Multiple Myeloma

In multiple myeloma, there is an urgent need for a precise risk stratification to assist in therapeutic decision-making. While many patients do well with the standard of care, a minority of patients rapidly progress.

Celgene partnered with Sage Bionetworks, a non-profit biomedical research organization, to bring together seven academic medical centers, non-profit patient advocacy groups and industry partners to organize and collect over a petabyte of molecular data on over 3,000 de-identified multiple myeloma patients. Sage Bionetworks hosted a crowdsourced online challenge allowing Sage's community of 20,000 research scientists to utilize the largest multiple myeloma data set assembled to date to better define molecular markers of high risk. The challenge succeeded in identifying a new high-risk signature. Furthermore, Sage Bionetworks continues to host the data allowing future groups to access and benchmark their novel signatures on the data set. This means that the work and time spent creating this collaboration and data set will continue to serve the multiple myeloma research community for years to come.⁵²



Rebates and other discounts reduced the average price growth for brand medications in the U.S. by nearly three-quarters in 2018⁵¹



Source: IQVIA National Sales Perspectives, Sep 2018, CPI projections from Economist Intelligence Unit (EIU), Aug 2018; IQVIA Institute, Dec 2018

Notes: 2018 Invoice price growth to YTD September 2018; Estimated net price growth in 2018 and forecast periods based on expected base case scenarios and interim review of selected company financial results; Protected Brands excludes new brands marketed less than 24 months in each year as price growth cannot be calculated.

Report: The Global Use of Medicine in 2019 and Outlook to 2023. IQVIA Institute for Human Data Science, Jan 2019

The benefits of medical innovation are global, and Celgene believes that patients from countries of differing economic circumstances should be able to benefit from these innovations. At the same time, the costs of innovation should be shared according to the financial circumstances of a country, such as the relative per capita gross national income. A flexible model that allows for differentiated prices according to an economy's ability to pay is therefore required to maximize patient access and sustain investment in R&D. Pricing flexibility supports broad patient access and strengthens each region's healthcare system to provide better outcomes for more people. This is the best way that we can maximize the value that Celgene products deliver to the healthcare system as a whole.

Celgene Patient-Centered Principles on Value Assessments

Celgene Patient-Centered Principles on Value Assessments are rooted in the company's long-held belief that value should be assessed holistically and over the long term, accounting for the following four value pillars: value to patients, value to the health system, value to society and the economy, and value to future innovation. The ultimate goal of Celgene Patient-Centered Principles on Value Assessments is to optimize access to therapies for all patients who stand to benefit. These principles are as follows:

1. Value assessments should be patient-centered

- Measure patient-relevant outcomes, accounting for varying treatment responses, preferences, needs and values
- Allow for consistent, timely and active involvement of patients and other relevant stakeholders throughout the process

2. Value assessments should be multi-dimensional

- Consist of a definition of value that considers value to patients, the health system, society and the economy, and future innovation
- Utilize a broad range of relevant and reliable evidence to capture the full spectrum of value
- Appropriately account for disease- and product-specific factors in the appraisal of the evidence

3. Value assessments should yield timely, high-quality outputs through flexible and transparent processes

- Deliver timely decisions that facilitate patient access to new treatments
- Ensure use of flexible processes that yield high-quality outputs
- Guarantee transparency in assessment processes and outputs

By the Numbers

Value to the Health System

~4,000

Medicines in development by the biopharmaceutical industry in the United States⁵³

225

Celgene-sponsored clinical trials underway⁵⁴

47,640

Patients currently enrolled in Celgene-sponsored studies⁵⁴

47

Compounds in Celgene-sponsored clinical trials⁵⁴



Value to the Economy and Society

“When determining value, we need to consider the positive impact of a medicine on society, such as the benefits to the caregiver and family of the patient, the potential reduction in other healthcare costs, the ability of patients to return to work, increases in economic productivity, and the overall positive impact of innovation on social and economic welfare.”

– Principles for the Pricing of Innovative Medicines

Value to the Economy and Society

Increased investment in biopharmaceuticals over the past 20 years has produced impressive results for patients, for the healthcare system, and for society overall. People are living longer and better, businesses have more productive employees, and society benefits from the value that these treatment advances provide.

Celgene considers value to the economy and society as a combination of:

- Increases in patient productivity
- Contributions to local, regional, national and global economies
- Benefits to families and caregivers of patients

While economic and societal value can be highly dependent on local circumstances, varying government policies, and the priorities, demographics and health of each community, expanding access to innovative medicines represents one of the most important ways for Celgene and other biopharmaceutical companies to impact health everywhere.

One of the ways that Celgene enables value to be realized is to ensure prices remain flexible to account for differing economic situations. The costs of innovation should not prohibit lifesaving or life-changing therapies from reaching people who can benefit in places where per capita income is lower. At the same time, reduced prices in economically challenged countries should not be used as benchmarks for prices in countries that have greater ability to pay, as doing so would stifle the very

innovation that enables these treatments to reach patients in the first place.

The variations in healthcare regulation and the structure of how healthcare is delivered also impact both prices and value. In places where government regulations can have an impact on which drugs are accessible to patients, the ultimate value of innovative therapeutics depends on factors well beyond Celgene or any biopharmaceutical company's control.

However, even with such limitations, the overall value of innovative medicines to the economy and society is substantial. Better health across society means increased productivity and – over time – lower healthcare costs. Indeed, innovative drugs that reduce hospitalization

mean that patients and their caregivers have more healthy, productive days. This provides value to them, to their families and to others who depend on them. Avoiding lost work, lost wages and lost ability to care for their loved ones provides value to these families.

As just one example, innovative treatment options for people with MS have accelerated over the past decade to help these 2.5 million patients worldwide live better each day.⁵⁵ At the same time, there are hundreds of thousands of patients who cannot obtain effective treatments, either because they cannot afford them or they do not have access to properly skilled healthcare providers or equipped clinics.⁵⁶ Moreover, changing insurance coverage has adversely affected access to treatment for people with MS. For instance, the practice of “step therapy” is growing — which forces people to

Global Focus: Celgene Cancer Care Links™

According to the World Health Organization, approximately 70 percent of cancer deaths occur in countries with limited economic resources.⁵⁷ Many of these countries, which span Asia, Africa and Latin America, face burdens, from poverty and food insecurity, to fulfilling basic needs, making cancer prevention, diagnosis and treatment services inconsistently available or lacking in critical support. While many organizations with oncology expertise are willing to share their knowledge and resources with these areas, additional support may be needed to connect these resources with programs in need.

To help address cancer care gaps in resource-constrained countries, Celgene launched Celgene Cancer Care Links™ in December 2017. This program provides competitive grant funding to local communities and institutions focused on enhancing patient care and building sustainable cancer care systems. The program aims to enhance cancer care and funds oncologist, pharmacist and nurse training programs; cancer prevention, detection and treatment services; and general medical education support.

In 2018, Celgene awarded 10 programs with more than \$1 million in total funding to expand essential cancer care services and support healthcare capacity building in resource-constrained countries. The awards support established institutions partnering with in-country medical centers that provide essential cancer care services including awareness and education, prevention, diagnosis and care.

Celgene Cancer Care Links™ is one example of how Celgene is partnering with stakeholders around the globe to change the course of human health for all humans, whether they live in developed or developing communities.



take medication that may not work for them before they can gain access to the treatment prescribed by their physician. In 2005, 27 percent of employer-sponsored plans reported using step therapy, and in 2014, the percentage had increased to 69 percent.⁵⁸ This increase represents the need for collaboration across multiple stakeholder groups so that the benefits of modern medicine are not limited only to those who can afford it.

In addition to the increased productivity and the economic benefits from reduced sick leave,

fewer hospitalizations and less use of other costly services, biopharmaceutical companies have a direct impact on the economy. Companies such as Celgene that invest much of their revenue in new R&D are job creators. Celgene employs not only scientists and other direct employees, but we indirectly contribute to job growth via the thousands of workers who build, operate and maintain Celgene facilities, as well as support the many vendors and other businesses that are a part of the communities in which Celgene operates.

	DISCOVERY			DEVELOPMENT			
	Hit ID	Lead ID	Lead Optimization	DC	Non-Clinical	Phase I	Phase II
DISEASE							
Visceral Leishmaniasis	[Progress bar]						
Cutaneous Leishmaniasis	[Progress bar]						
Chagas Disease	[Progress bar]						
Malaria	[Progress bar]						
Filariasis	[Progress bar]						
Tuberculosis	[Progress bar]						
Cryptosporidium	[Progress bar]						
Viral/Bacterial Infections	[Progress bar]						
PDE4 INHIBITOR (CC-11050)							
Tuberculosis	[Progress bar]						
Erythema Nodosum Leprosium	[Progress bar]						
HIV PK/Safety Study	[Progress bar]						
POMALIDOMIDE							
Kaposi Sarcoma	[Progress bar]						

Celgene Global Health Pipeline: Research with a Mission to Transform Treatment for Neglected Diseases⁵⁹

In 2009, Celgene established Celgene Global Health (CGH), a unit dedicated to developing transformative medicines for neglected diseases to improve the lives of patients in resource-constrained countries. Celgene has a portfolio of over 400,000 compounds across multiple platforms that have the potential to treat diseases such as malaria, tuberculosis, Chagas, leishmaniasis and others.⁵⁹ CGH is partnering with academic, nongovernmental and other public and private entities around the world to evaluate these compounds as potential treatments for neglected diseases. Many of these diseases provide daunting challenges — tuberculosis has infected about 2 billion people and caused 1.8 million deaths;⁶⁰ in 2016, there were 212 million new cases of malaria reported;⁶¹ and in 2015, there were 200,000 new cases of leprosy, which causes permanent damage to skin, nerves, eyes and limbs.⁶² CGH engages in discovery, development and lead optimization with the goal of delivering new treatments to patients who have limited treatment options.



By the Numbers

Value to the Economy and Society

4.7 million

Jobs in the United States supported by research-based biopharmaceutical companies in 2015⁹

88+

Countries in which Celgene is serving patients⁵⁹

8,800+

Celgene employees globally as of December 31, 2018⁵⁴

Across the biopharmaceutical industry, **over 800,000** employees in the United States, as of 2018, and **over 700,000** employees in Europe, as of 2016, go to work every day to create new treatments and cures for patients⁶³



Value to Future Innovation

“Changing the course of human health through bold pursuits in science, and a promise to always put patients first.”

– Celgene Purpose

Value to Future Innovation

Celgene's innovations available to patients today are the result of decades of effort and investment. Future innovation requires this commitment to continue and grow. As a company dedicated to R&D, everything Celgene does is with an eye toward its impact on the future – not just innovative therapies but also new technologies, research methods and fundamental insights into human health and important diseases. Taken together, this is how we deliver maximum value to the most people around the world.

At Celgene, we consider value to future innovation as:

- Investment in discoveries about existing medications
- Investment in medical innovation for new therapies addressing significant patient need
- Contribution to the development of a competitive yet collaborative medical R&D ecosystem

This definition represents a continuous loop of research, innovative new products, and more research using revenue from those new products to support the continuing cycle of innovation. This virtuous cycle of innovation also generates highly valuable jobs.

Compared with other industries, the biopharmaceutical sector invests more in R&D than any other. In the United States alone, biopharmaceutical companies invested \$65 billion in R&D in 2016.⁶⁴ Globally and across all industries, Celgene ranks as the third biggest corporate investor in terms of R&D intensity, measured as the percentage of revenues reinvested into R&D.¹⁰

Continuous investment, powered by the revenue of existing innovative products, has far-reaching impact and value. We are seeing the fruit of this investment today as treatments for cancer transform into truly personalized medicines that harness the body's own cells and direct them to interrupt tumor growth. Precision medicine has the potential to revolutionize how healthcare is provided and diseases such as cancer, diabetes and heart disease are diagnosed, treated and prevented. However, the value is only meaningful if patients have access to the therapies they need.

In the past two years, cancer therapies that convert chimeric antigen receptor T (CAR T) cells into cancer-fighting cells have emerged as one of the most exciting developments in the decades-long war against cancer. CAR T is an FDA-approved cell therapy for the treatment of certain blood cancers that have not responded or have stopped responding to prior treatments

and has shown potential in other types of blood cancers in clinical studies.⁶⁵ Celgene CAR T therapies are in development and are not yet approved by the FDA. While Celgene works to be a leader in CAR T and deliver on this commitment to innovation, we also realize that access barriers remain before more people can access these therapies.⁶⁶

Operationally, the production of approved CAR T cell therapies is complex, as each treatment is engineered from an individual patient's cells before being infused into the patient. The process requires an unprecedented level of collaboration between physicians, health centers and biopharmaceutical innovators.

Another significant obstacle to patient access exists — reimbursement. These personalized therapies do not fit neatly into existing private payor or government payment models, including Medicare, meaning potential delays for patients and complications for providers while they strive to find a solution.⁶⁶

In other words, future innovation requires not just advanced biopharmaceutical science. It also requires innovation in how health plans and other payors evaluate and pay for treatments. Celgene is working to convene these critical conversations and is actively collaborating with relevant stakeholders to develop new approaches to deliver value across the healthcare system.

Collaborating with stakeholders also gives us a greater understanding of how different treatments work in different patients and how treatments work once they have gone beyond the boundaries of clinical research and into patients in real-world medical practice. Celgene has made a major commitment to forward-looking research that can help healthcare providers know which treatments work best for their patients using deidentified data from pharmacy, hospital and other electronic medical records, to case reports and other sources, with the goal of identifying possible adverse reactions as quickly as possible.

For patients using Celgene investigational products, we are developing new ways to use technology to enhance how we monitor for the potential of adverse drug reactions. The risks and benefits of biopharmaceutical products are continuously evaluated, and key decisions are taken to ensure the safety of patients. Through Chrysalis, Celgene's progressive pharmacovigilance innovation program, we are working with researchers to develop artificial intelligence that can speed the review of the increasing number of individual case safety reports, with the goal of detecting, assessing, understanding and, where possible, preventing adverse events and any other drug-related problems. We want to transform pharmacovigilance by introducing innovative approaches that leverage artificial intelligence and machine learning to increase operational efficiency, consistency, quality of data collection, and signal detection.

Technologies like artificial intelligence also help us make drug development more effective and efficient, potentially shortening development timelines. New digital tools can empower clinical researchers, laboratory scientists, physicians and patients to discover new insights and



manage health better.

The combination of widespread electronic health records, nearly ever-present smartphones, and wearable health monitoring devices enables researchers to collect and analyze a vast amount of information about patients that was never before accessible. Celgene supports and uses these technologies to better understand patients and drive future innovation.

In another collaboration with Sage Bionetworks, Celgene supported research that used an iPhone®-based app and wearable technology to collect measurements and self-reported data on the impact of chronic anemia due to myelodysplastic syndromes (MDS), myelofibrosis and beta-thalassemia on daily life. Researchers hope to use this information to evaluate new treatments for reducing the impact of these diseases on patients by assessing quality of life measures as well as important disease markers from the patient's blood. This is science that benefits everyone involved in biopharmaceutical research and the health system at large, not just Celgene.

Future innovation extends beyond traditional biopharmaceutical research. Precision medicine, with its ability to pinpoint patients most likely to benefit from specific treatment approaches, has the potential to speed the time that new medicines take to get from bench to bedside. New medicines still average 14 years from patent filing to approval, but recent cancer treatments have made it through clinical research and regulatory approval faster.⁶⁷

In order for innovation to be meaningful, it must be continuous. Celgene supports research to identify how treatments work in the real world, and that data inform scientists working to develop the next breakthrough therapies. ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) has helped change the standard of care for people diagnosed with metastatic pancreatic cancer, one of the deadliest and hardest to treat cancers. However, efforts to realize even more benefit in this disease proceed in earnest.

The same is true for patients with multiple myeloma, which remains an incurable cancer despite significant progress to date — only half of patients survive five years after diagnosis.⁶⁸ In recent years, REVLIMID® (lenalidomide) has become available for maintenance treatment for patients with multiple myeloma after autologous hematopoietic stem cell transplantation. REVLIMID as maintenance therapy was studied in two clinical trials. In the first study, conducted in the United States, REVLIMID maintenance therapy extended the median progression-free survival by 3.8 years compared to no maintenance therapy.⁶⁹ In the second study, conducted in Europe, REVLIMID maintenance therapy extended the median progression-free survival by 1.9 years compared to no maintenance therapy.⁶⁹ For patients with relapsed and refractory multiple myeloma, POMALYST® (pomalidomide) is approved for treatment in combination with dexamethasone in patients who have failed two other therapies. In a clinical study, the median progression-free survival of POMALYST in combination with dexamethasone was two times longer than dexamethasone alone (3.6 months compared to 1.8 months).⁷⁰

While the progress Celgene has been able to achieve to date has helped change the prognosis for patients with certain types of cancer, we are far from satisfied. Celgene will continue intensive R&D efforts until cancer is a manageable chronic condition and hopefully one day cured. These successes give reason for optimism about the significant value of future innovation to all stakeholders, but it requires an ongoing and substantial commitment. Not only does new drug development necessitate considerable time and resources, it is risky.⁷¹ On average, a drug costs \$2.6 billion to develop, and only 3.4 percent of investigational cancer treatments will ever win FDA approval; however, what we learn from those drugs that fail advance the knowledge of human health in other ways.⁷² The body of knowledge developed by biopharmaceutical companies collectively informs future innovation. That is one of the most important forms of value that Celgene produces.

Q&A on CAR T

Q: What are some of the existing barriers that prevent patients who may benefit from FDA-approved CAR T therapies from receiving access?

Right now, there are limited numbers of institutions that are set up to deliver CAR T cell therapy to patients. This means that for patients with both commercial insurance and Medicare, there are barriers to access simply because of the need to travel long distances to find an institution that is certified to deliver FDA-approved CAR T therapies. A primary goal for Celgene as we continue researching and developing CAR T therapies is to work toward the expansion of geographic access to CAR T therapy for patients beyond the limited sites that currently deliver it. As previously noted, Celgene CAR T therapies are still in development and are not approved by the FDA.

For Medicare beneficiaries, there are additional challenges that are unique to the Medicare program. To date, the inpatient reimbursement rates that institutions receive to deliver CAR T are inadequate. We believe this inadequate reimbursement is restricting access for some Medicare beneficiaries, which can make it disproportionately easier for commercially insured patients to access CAR T therapies when compared to Medicare patients.

Q: What is Celgene doing to address these access barriers?

Celgene is working with a diverse group of stakeholders, including provider organizations, patient organizations and industry colleagues, to identify and define alternative reimbursement mechanisms in the inpatient setting. Celgene believes these alternative mechanisms are a better fit given the unique nature of CAR T therapy and its transformative potential for patients.





Value in Action: The Impact of Precision Medicine

Precision medicine has become a major focus in how medicines are researched, and diseases are diagnosed and treated. The value of precision medicine for patients is clear — these targeted therapies can be effective when treating the right patient.⁷³

Precision medicine also enables future innovation by revealing additional potential targets for future R&D. As we learn more about the underlying genomics of the human body and certain diseases, we gain insights into how diseases express themselves in the body, which helps researchers find new pathways for research, development and future treatment.⁷⁴ Additionally, precision treatments have the ability to control the overall cost of healthcare by shifting the emphasis in medicine from reaction to prevention by identifying the molecular signals of disease that present themselves before the physical symptoms appear.⁷⁴

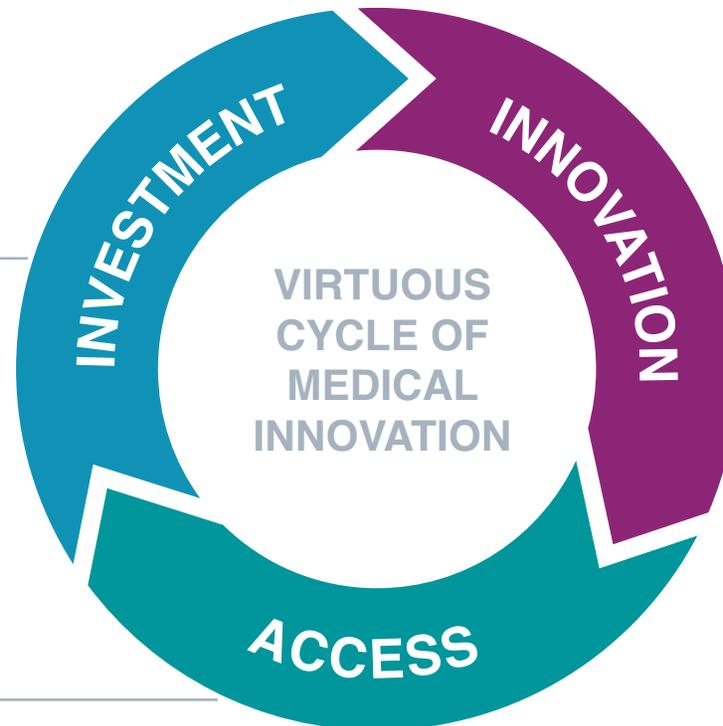
There are currently 132 precision medicines on the market, and approximately 75,000 genetic tests available that could potentially guide the use of precision treatments.^{73,74} Additionally, 42 percent of the drugs in development include a biomarker as part of their R&D studies.⁷⁴

As biopharmaceutical companies focus on medicines that are specialized to each individual's genetics or biology, investment in the fields of immunotherapy and cell and gene therapies is expected to increase by at least 33 percent over the next five years, potentially revolutionizing how disease will be treated.⁷⁴

The Virtuous Cycle of Medical Innovation

Access and reimbursement for innovation today make possible the investment in R&D that leads to future medical advances.

Celgene has invested on average 39% of revenue in R&D during the past five years.



Continuous investment of time and resources by biopharmaceutical companies such as Celgene leads to new medical breakthroughs.

Access and reimbursement for innovative therapies fund investment in future medical advances.

By the Numbers

Value to Future Innovation

39%

Average percentage of revenues reinvested by Celgene over the last five years⁵⁴

* Numbers based on Generally Accepted Accounting Principles

2,460

Investigator-initiated trials that involve Celgene products as of March 2019⁵⁴

400,000

Compounds made available by Celgene to the Drugs for Neglected Diseases Initiative (DNDi)⁵⁴

12

Celgene active clinical programs in inflammatory and immunology disease⁷⁶

9

Celgene active clinical programs in multiple myeloma⁷⁶

10

Celgene active clinical programs in myeloid disease⁷⁶

13

Celgene active clinical programs in solid tumors⁷⁶

9

Celgene active clinical programs in lymphoma and leukemia⁷⁶

CLOSING CASE STUDY

CAR T: A PARAGON OF VALUE & INNOVATION

Although Celgene CAR T therapies are investigational and not yet approved, these cell therapies provide a compelling illustration of the Celgene approach to value. CAR T cell therapies demonstrate how it is possible for years of research and development to yield value for patients, the health system, the economy and society, and future innovation.

VALUE TO PATIENTS

CAR T is a cell therapy that uses a patient's own cells to create a therapy capable of strengthening the immune system and attacking cancer cells.¹ CAR T cell therapy is a treatment that has the potential to change treatment paradigms in patients with certain types of blood cancers. The first CAR T cell therapy was approved by the FDA in 2017.² An additional 289 cell or gene therapies are in development with the potential of treating over 100 different diseases.¹



VALUE TO HEALTHCARE SYSTEM

Treatments like CAR T cell therapy are highly effective in certain patient populations and mean that healthcare budgets can be refocused on to other services and treatments leading to more efficient healthcare spending.



VALUE TO ECONOMY & SOCIETY

CAR T cell therapies offer the potential for durable responses, saving on costs associated with the treatment of a disease.



VALUE TO FUTURE INNOVATION

Yesterday's innovations have paid for today's innovations, including CAR T cell therapy. For Celgene, in particular, the ongoing development of CAR T cell therapies would not have been possible if it were not for the commercial success of REVLIMID, POMALYST, OTEZLA and the other therapies that Celgene has brought to market in recent years. And CAR T cell therapies available to patients today or in the coming years will help pay for future innovation.



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