



PHARMACEUTICAL **POLICY PASSPORT**

Understanding pharmaceutical innovation
to improve access to new treatments



Today, MSD is at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world.

We will continue to lead the charge to cure diseases for which there are no cures or even good treatments, and diseases that are sure to emerge. Our quest won't end until our inventions move many more devastating diseases from homes and hospitals into history books.

Dr. Susanne Fiedler, Senior Vice-President Europe & Canada

WHY A POLICY PASSPORT?

At MSD, we believe that pharmaceutical innovation is the result of a sophisticated ecosystem that mixes investments in science, adequate healthcare spending, and industrial policy focused on building a knowledge economy.

The European Union and governments in Europe play a key role in the creation and sustainability of this ecosystem. Supporting investment in fundamental science, financing healthcare, and implementing industrial policies focused on innovation (such as intellectual property rights) are critical to enable pharmaceutical companies like MSD to deploy their research and development (R&D) efforts and develop innovative treatments for EU patients.

This document is intended to provide policy makers with a “roadmap” of the drivers and critical policies that support pharmaceutical innovation. It is this web of government policies that provided the conditions for pharmaceutical companies to invest over €36.5 billion in research and development in the EU alone in 2018.¹

I want to thank my team at the MSD Brussels Policy Centre for producing this Policy Passport, with special thanks to Boris Azaïs, Director Public Policy and Bjelle Roberts, Assistant Specialist Public Policy Vaccines.

David Earnshaw,
Associate Vice-President
MSD Brussels Policy Centre

IN THE EU, WE HAVE THE
SCIENCE, THE HEALTH
SYSTEMS, AND THE
PHARMACEUTICAL COMPANIES
TO CONQUER DISEASE AND
PROVIDE BETTER HEALTH
TO OUR CITIZENS



¹ EFPIA, The Pharmaceutical Industry in Figures – Key Data 2019



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EUROPE IS THE ORIGINAL BIRTHPLACE OF PHARMACEUTICAL INNOVATION

Progress in science, industrial entrepreneurship, and nascent public health thinking paved the way for modern pharmaceutical innovation to start in Europe at the end of the 19th century.

Pharmaceutical innovation has been one of the driving forces behind the tremendous progress in life expectancy and better health we have experienced in the last 60 years.¹

After clean water and sanitation, the development of novel health technologies by pharmaceutical companies has been a key driver of healthier and longer lives.

Just to cite a few - antibiotics, vaccines, cardiovascular medicines, diabetes medicines, antiretroviral against HIV/AIDS, hepatitis C cures, and breakthrough cancer medicines are among the new treatments that have helped us achieve critical progress in healthcare.

POLICY MAKERS PLAY A CRITICAL ROLE IN STRENGTHENING THE EU LEADERSHIP IN PHARMACEUTICAL INNOVATION



BUT WHAT DRIVES PHARMACEUTICAL INNOVATION?

How do we make the link between fundamental science and a pill that will help patients?

Policy makers can create the legislation that supports the long pathway between a scientific discovery published in a scientific journal and the prescription filled for a patient at a pharmacy.

¹ Lichtenberg, Frank, "The Impact of New Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level Data from 52 Countries, 1982–2001". 2005. International Journal of Health Care Finance and Economics.



A KNOWLEDGE-BASED ECONOMY CONNECTS SCIENCE, HEALTH, AND INDUSTRY



BETTER HEALTH FOR EUROPEAN CITIZENS THROUGH PHARMACEUTICAL INNOVATION IS THE RESULT OF THIS UNIQUE POLICY MIX



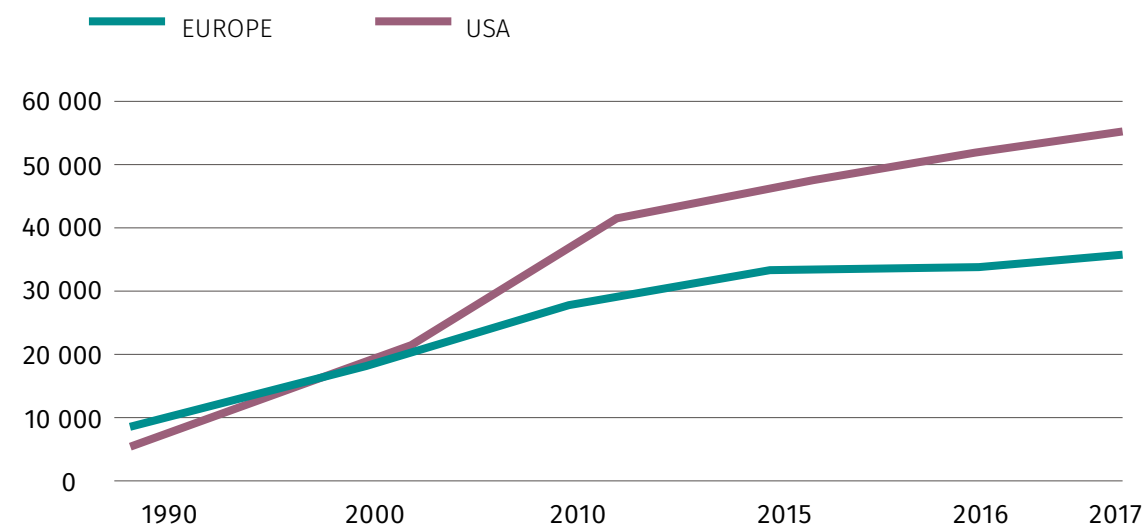
EUROPE NEEDS MORE R&D

The research-based pharmaceutical industry is one of the leading high-tech sectors in Europe. Europe remains a global source of new medicines, but is losing pace to global competitors. As a knowledge-based economy, Europe has all the ingredients to regain its global leadership, provided that we continue to implement the appropriate policy mix of strong science, investment in health-care and a robust incentive framework.

OUR MAIN MESSAGE, AND VISION, IS THAT INVESTING IN RESEARCH AND INNOVATION IS INCREASINGLY CRUCIAL FOR SHAPING A BETTER EUROPEAN FUTURE IN A RAPIDLY GLOBALISING WORLD, WHERE SUCCESS DEPENDS EVER MORE ON THE PRODUCTION AND CONVERSION OF KNOWLEDGE INTO INNOVATION.

Pascal Lamy in "Investing in the European future we want", Report of the independent High Level Group on maximising the impact of EU Research & Innovation Programmes, 2017.

PHARMACEUTICAL R&D EXPENDITURE IN EUROPE AND USA
MILLION OF NATIONAL CURRENCY UNITS



Source: EFPIA, Pharmaceutical industry in figures, 2019.



HOW CAN THE EU REGAIN ITS LEADERSHIP?



R&D IMPROVES HEALTH

Since 1950, more than 1,400 new drugs have been approved.¹ This wave of innovation has played a key role in the steady increase in life expectancy.²

Pharmaceutical innovation provides numerous benefits to different healthcare stakeholders. In addition to health gains, pharmaceutical innovation brings greater societal benefits such as releasing other healthcare resources (for example, antiretroviral therapy against HIV/AIDS freed up

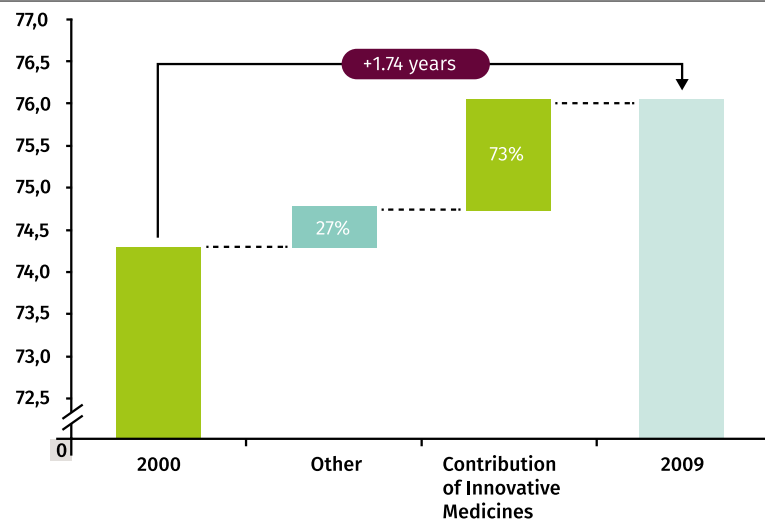
hospital wards), increasing work force productivity and improving macroeconomics through greater investment in human capital.

In a study covering 2000–2009 across 30 OECD countries, innovative medicines are estimated to have contributed to 73% of the 1.74 year improvement in population weighted mean life expectancy at birth after accounting for other factors.³

NOBEL PRIZE-WINNING ECONOMIST GARY BECKER CALLED LONGER LIFE ACHIEVED THROUGH NEW MEDICAL INNOVATION ‘THE LAST CENTURY’S GREATEST GIFT’

Kumar, V. & Sundarraj, R., Global Innovation and Economic Value (2018).

CONTRIBUTION OF INNOVATIVE MEDICINES TO INCREASE IN LIFE EXPECTANCY



1 Kinch M. et al., “An Overview of FDA-Approved New Molecular Entities (NMEs): 1827-2013”, Drug Discovery Today, 2014.

2 Lichtenberg F., “The Impact of New Drug Launches on Longevity: Evidence from Longitudinal, Disease-Level. Data from 52 Countries, 1982–2001”, International Journal of Health Care Finance and Economics, 5, 47–73, 2005.

3 Lichtenberg, F., “Pharmaceutical innovation and longevity growth in 30 developing OECD and high-income countries, 2000–2009”, 2012



R&D PROMOTES ECONOMIC GROWTH

2.5 million jobs are supported by the pharmaceutical sector in Europe, contributing €206 billion in Gross Valued Added in 2016.¹ This amounts to an average Gross Value Added per employee of €156,000 which is significantly higher than other key sectors. Overall, the activities of the pharmaceutical companies directly contributed nearly €100 billion to EU economies in 2016, with an additional €106 billion provided through the supply chain and employee spending.¹

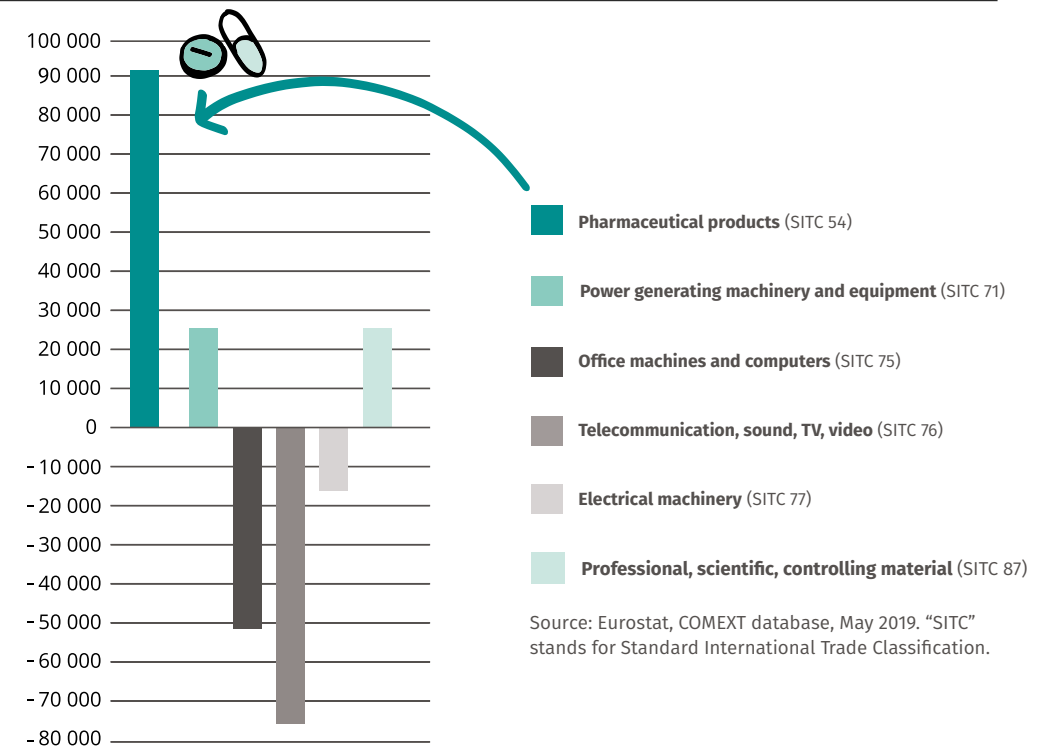
Research-based pharmaceutical companies also contributed over €91 billion to the EU trade surplus and invested €36.5 billion in R&D in Europe alone in 2018.²

THE TRADE SURPLUS IN PHARMACEUTICAL AND MEDICINAL PRODUCTS GREW FROM €22 BILLION IN 2002 TO A RECORD HIGH OF €91 BILLION IN 2018.

EUROSTAT, International trade in medicinal and pharmaceutical products. Data from May 2019.

EU-28 TRADE BALANCE – HIGH TECHNOLOGY SECTORS

€ Million – 2018



Source: Eurostat, COMEXT database, May 2019. “SITC” stands for Standard International Trade Classification.

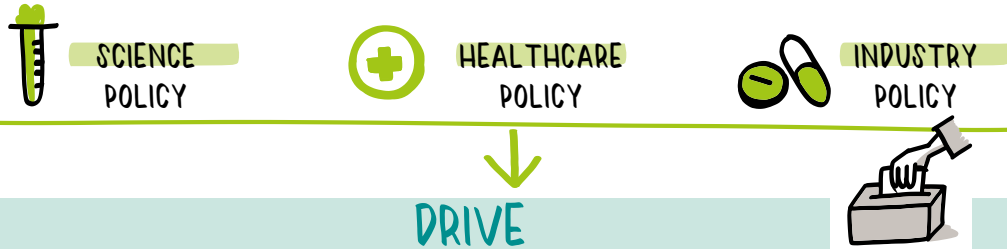
1 PwC/EFPIA, “Economic and societal footprint of the pharmaceutical industry in Europe”, June 2019

2 EFPIA, “The Pharmaceutical Industry in Figures – Key Data 2019”. R&D spending in 2018 is estimated. It was €35.3 billion in 2017 and €33.9 billion in 2016.



POLICY MAKERS ARE IN THE DRIVING SEAT

THE THREE KEY POLICY PILLARS



INVESTMENTS IN SCIENCE:

- Basic science
- Higher education
- Academic centres
- Public-private partnerships

INVESTMENTS IN PUBLIC HEALTH:

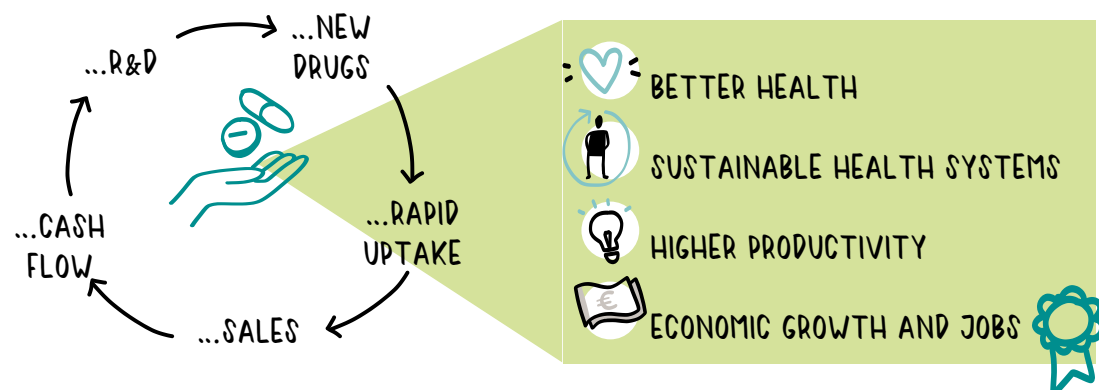
- Health financing
- Patient centricity
- Evidence based medicine
- Focus on value
- Rapid access for patients

FAVOURABLE BUSINESS ENVIRONMENT:

- Intellectual Property
- Research tax credits
- Stable regulatory framework
- Reward innovation

NEW TREATMENTS

POLICY OUTCOMES



THE SOURCE OF INNOVATION

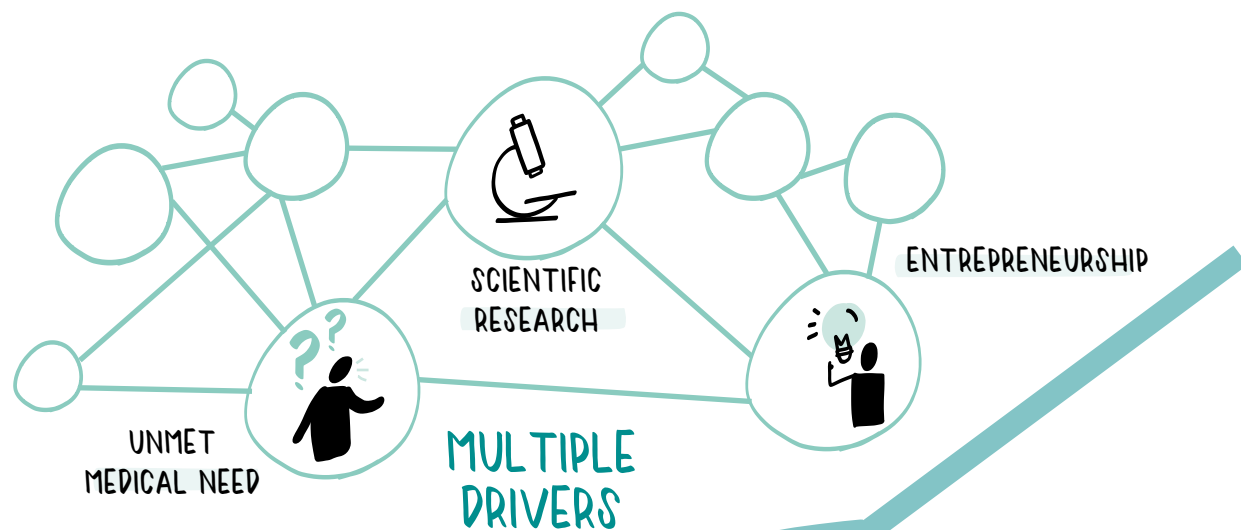
*Invention is 1% inspiration
and 99% perspiration.*

Thomas Edison



WHAT DRIVES PHARMACEUTICAL INNOVATION?

Pharmaceutical innovation is at the junction of **scientific advances**, **unmet medical needs** and **entrepreneurship**. These fundamental drivers are shaped by governments through strong “**enablers**”, such as intellectual property rights, uptake of new treatments by health systems and a pricing and reimbursement system that rewards innovation. This policy mix allows companies to engage in high-risk, high-cost research and development activities.



TODAY, close to **30** diseases are preventable by vaccination,

preventing between **2** and **3** million deaths globally per year

10 facts on immunization, WHO

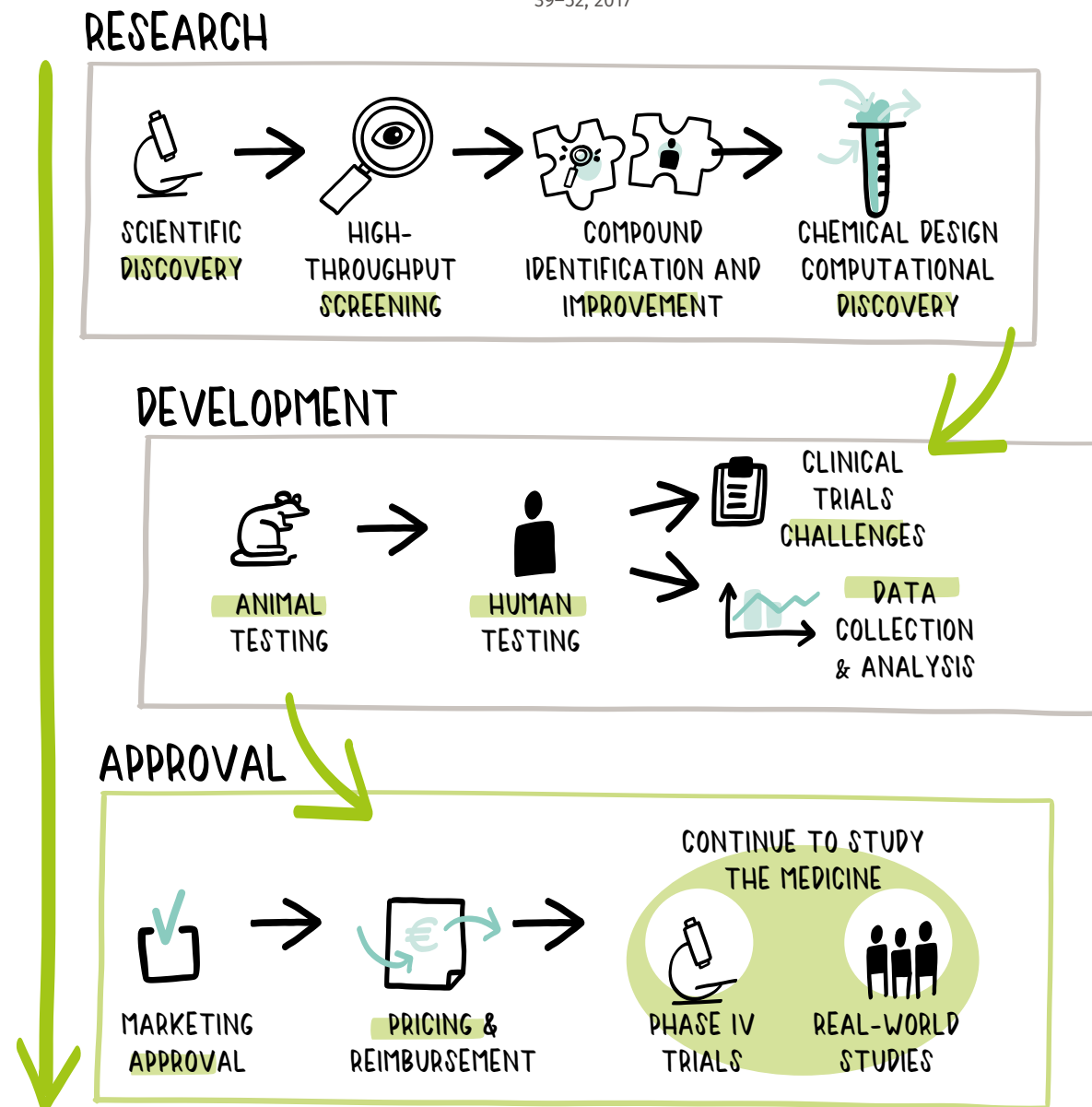
- ★ PARTNERSHIPS
- ★ INCENTIVES
- ★ PRO-INNOVATION REGULATION
- ★ PRICING THAT REWARDS INNOVATION



MEDICINES DON'T GROW ON TREES

IT TOOK ALMOST 25 YEARS BETWEEN THE DISCOVERY OF THE HEPATITIS C VIRUS AND THE LAUNCH OF SAFE, TOLERABLE, AND SIMPLE TREATMENTS THAT DELIVER OVER 95% CURE RATES

Adapted from Burstow et al., “Hepatitis C treatment: where are we now?”, *International journal of general medicine*, 10, 39–52, 2017



AND ALL THIS TAKES ON AVERAGE



13 YEARS AND COSTS ABOUT **€2.33 BILLION**



USD 2.6b converted from USD at May 2019 rate

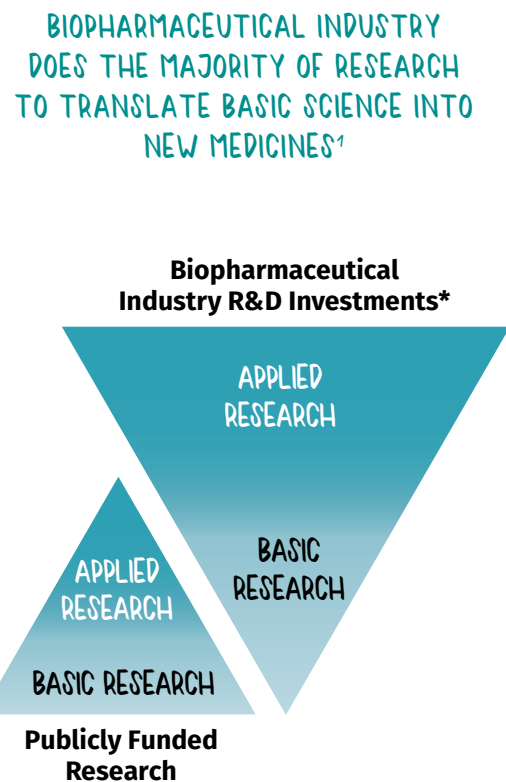
DiMasi JA, Grabowski HG, Hansen RW. “Innovation in the pharmaceutical industry: new estimates of R&D costs.” *J Health Economics*. 2016;47:20–33.



FROM THEORY TO THERAPY

From a scientific discovery to a drug that saves lives, public and private research laboratories play a complementary role in a very long series of increasingly expensive investments. From the publication of a paper at a scientific congress to the investment in clinical trials involving thousands of patients, the path to a pharmaceutical treatment will benefit from numerous inputs and contributions. Whilst public institutions and the private sector both focus on researching the causes, biological mechanisms and epidemiology of disease, the private sector further emphasises the actual discovery and development of new treatments that can be prescribed to patients.

Public and private research laboratories have increasingly collaborated in order to produce and translate knowledge, accelerate the discovery, development and production of innovative drugs.



OUR ANALYSIS INDICATES THAT INDUSTRY'S CONTRIBUTIONS TO THE R&D OF INNOVATIVE DRUGS GO BEYOND DEVELOPMENT AND MARKETING. THEY INCLUDE BASIC AND APPLIED SCIENCE AND DISCOVERY TECHNOLOGIES. WITHOUT PRIVATE INVESTMENT IN THE APPLIED SCIENCES, THERE WOULD BE NO RETURN ON PUBLIC INVESTMENT IN BASIC SCIENCE.

Chakravarthy R, et al., Therapeutic Innovation & Regulatory Science. 2016;50(6): 759-768.

* For a review of the division of labour between public and private research, please see Derek Lowe, "Where Drugs Come From: A Comprehensive Look", 28 May 2019. <https://blogs.sciencemag.org/pipeline/archives/2019/05/28/where-drugs-come-from-a-comprehensive-look>

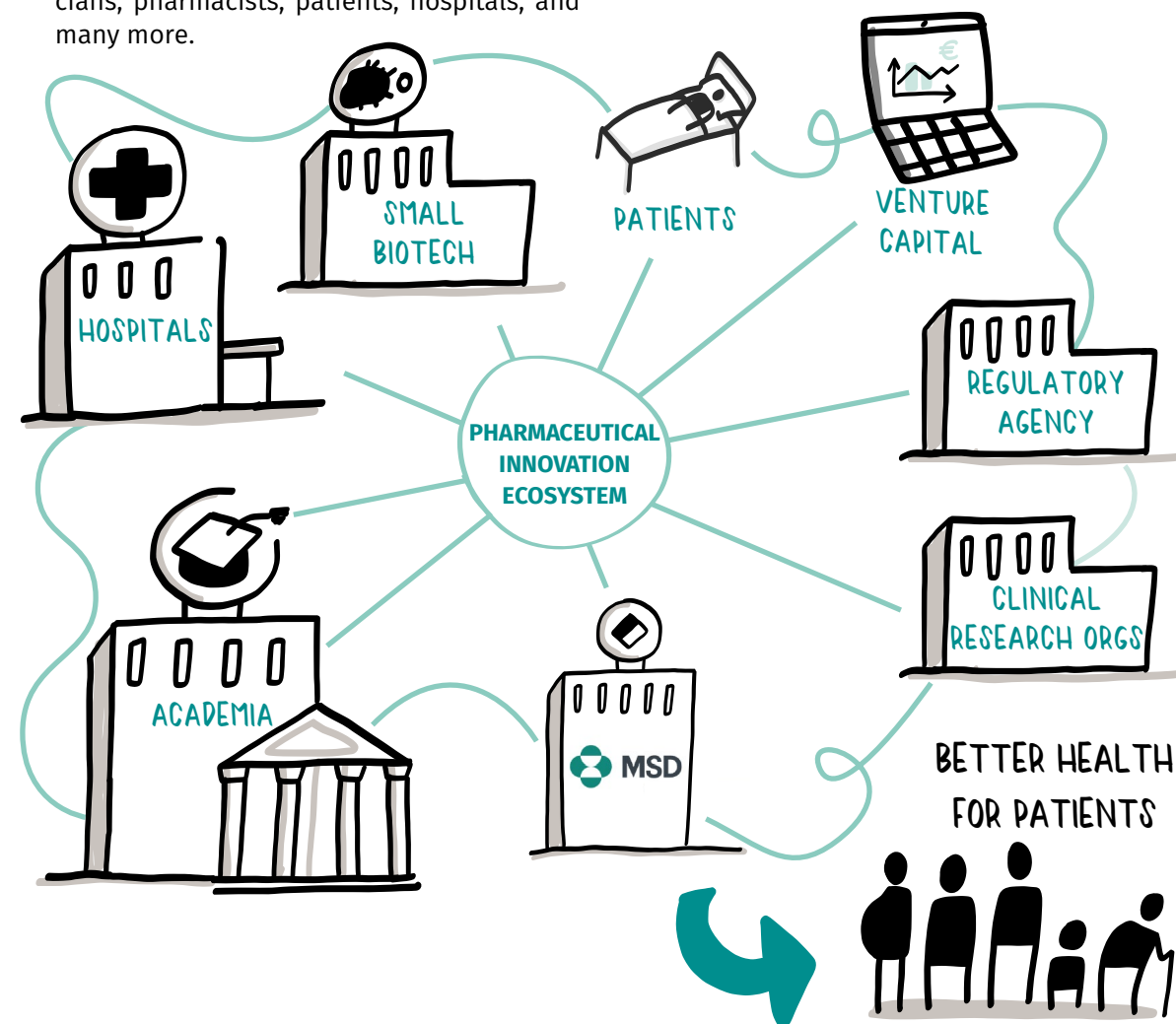
¹ Chakravarthy R, Cotter K, DiMasi J, et al. "Public and private sector contributions to research & development of the most transformational drugs in the past 25 years: from theory to therapy." Therapeutic Innovation & Regulatory Science. 2016; 50(6): 759-768.

IT TAKES A VILLAGE...

Pharmaceutical innovation results from a complex ecosystem with multiple public and private actors.

Through pro-innovation policies, the EU and national governments support the collective effort to turn science into new pharmaceuticals. There is a long list of actors and stakeholders including health authorities, regulators, universities, industry labs, physicians, pharmacists, patients, hospitals, and many more.

THE OVERALL OBJECTIVE OF ALL ACTORS IN THE DRUG R&D ECOSYSTEM IS TO ADVANCE MEDICAL SCIENCE AND TRANSLATE IT INTO NEW TREATMENTS





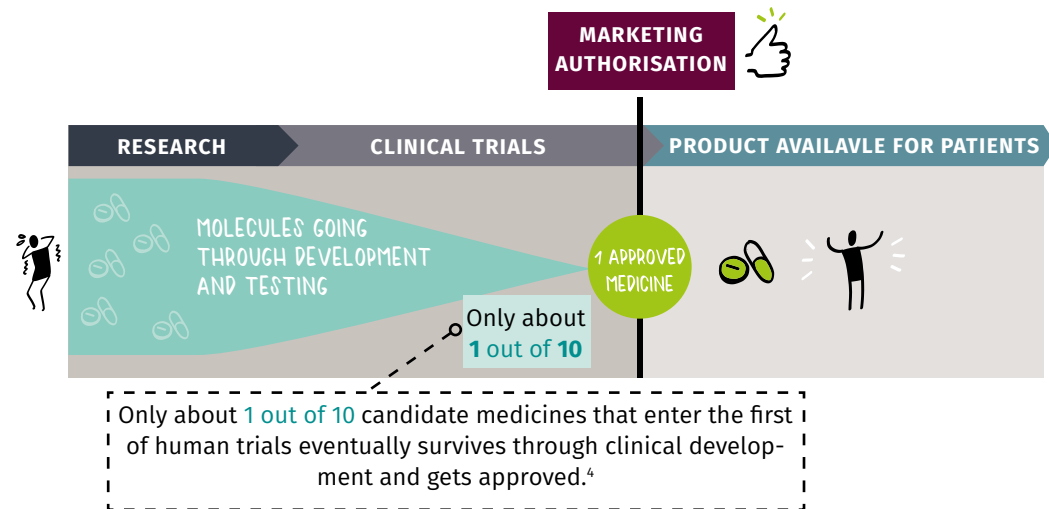
AGAINST GREAT ODDS WE CONTINUE TO INNOVATE

On average, the development of a new medicine takes 13 years and costs €2.33 billion.¹

To put this timeframe into perspective, it took over 20 years between the seminal scientific discoveries² that certain proteins can block the action of our immune system against cancer cells and the first regulatory approval of cancer treatments based on this insight. Another humbling illustration of the challenges faced by pharmaceutical innovators can be found in the 99% failure rate in R&D for Alzheimer's disease.³

Between 1998 and 2017, there were 146 unsuccessful trials to develop medicines to treat and potentially prevent Alzheimer's. In that same timeframe, only four new medicines were approved to *treat the symptoms* of Alzheimer's disease, but we still lack treatment addressing the *progression of the disease*. In other words, for every research project that succeeded, about 37 failed.³

Despite these setbacks, there are about 7,000 medicines in development globally, including for various types of cancer, neurological disorders, autoimmune diseases, and Alzheimer's disease.



¹ DiMasi JA, Grabowski HG, Hansen RW. "Innovation in the pharmaceutical industry: new estimates of R&D costs." J Health Economics. 2016;47:20-33.

² Adapted from press release for the 2018 Nobel Prize in Physiology or Medicine awarded for the discovery of cancer therapy by inhibition of negative immune regulation. <https://www.nobelprize.org/uploads/2018/10/press-medicine2018.pdf>

³ PhRMA, "Researching Alzheimer's Medicines - Setbacks and Stepping Stones." Fall 2018. Cummings J.L., et al. Alzheimer's disease drug-development pipeline: Few candidates, frequent failures. *Alzheimers Res Ther.* 2014.

⁴ Pharmaceutical Technology, Counting the cost of failure in drug development, 19 June 2017.



WE DON'T REST

Over decades, pharmaceutical companies have been able to relentlessly pursue new medicines to address unmet medical needs.

In 2018, pharmaceutical companies have launched globally a record number of 68 new active substances (NAS).¹

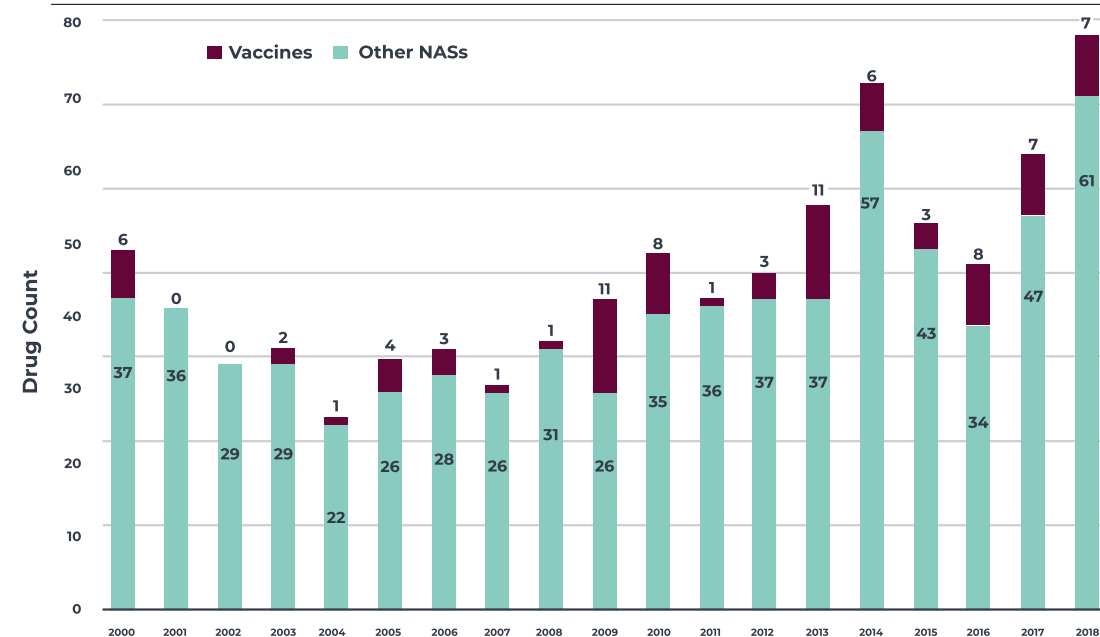
This was a record year, and historical figures show an average rate of 40 new treatments and vaccines since the start of the millennium.

This achievement is quite spectacular, since R&D costs have continued to increase during the last 15 years due to the increasing complexity of scientific challenges and increased regulatory requirements.²

FAR FROM BEING "BROKEN", THE PHARMACEUTICAL INNOVATION FRAMEWORK IS DELIVERING AT A CONSTANT PACE OVER DECADE-LONG CYCLES

759 INNOVATIVE MEDICINES AND VACCINES LAUNCHED SINCE 2000

Number of New Active Substances and vaccines launched per year¹



Source: Pharmaproject®, "Pharma R&D Annual Review 2019 Supplement", March 2019. <https://pharmaintelligence.informa.com/~media/informa-shop-window/pharma/2019/files/whitepapers/nas-supplement-whitepaper.pdf>

¹ "New Active Substances" refer to new chemical or biological entities that had received no prior approval. This excludes reformulated drugs or non-NAS moieties, or biosimilars. Pharmaproject® April 2019.

² DiMasi J., Grabowski H., Hansen R., "Innovation in the pharmaceutical industry: New estimates of R&D costs." *Journal of Health Economics*, 47 (2016), 20-33



THE CRITICAL ROLE OF INCENTIVES

Fundamentally, when inventing new treatments, pharmaceutical companies discover and produce knowledge about the properties of chemical and biological products in humans and demonstrate their treatment or curative value. This “knowledge” is extremely expensive to produce, but relatively easy to copy once the patent is published, and the clinical evidence has been produced through research and development efforts. This explains why innovative companies rely so much on intellectual property rights. Intellectual property rights represent the oxygen that enables innovative companies to raise capital and justify the significant investments required to invent a new medicine for patients. **Weakening incentives will not reduce prices: it will first reduce investments in developing new treatments and cures.**

At MSD, R&D expenses were \$10.2 billion in 2017 and \$10.1 billion in 2016. This represents an R&D “intensity” of 25% of our revenues.¹ This level of R&D investment puts MSD in the top 10 companies globally across all sectors.²

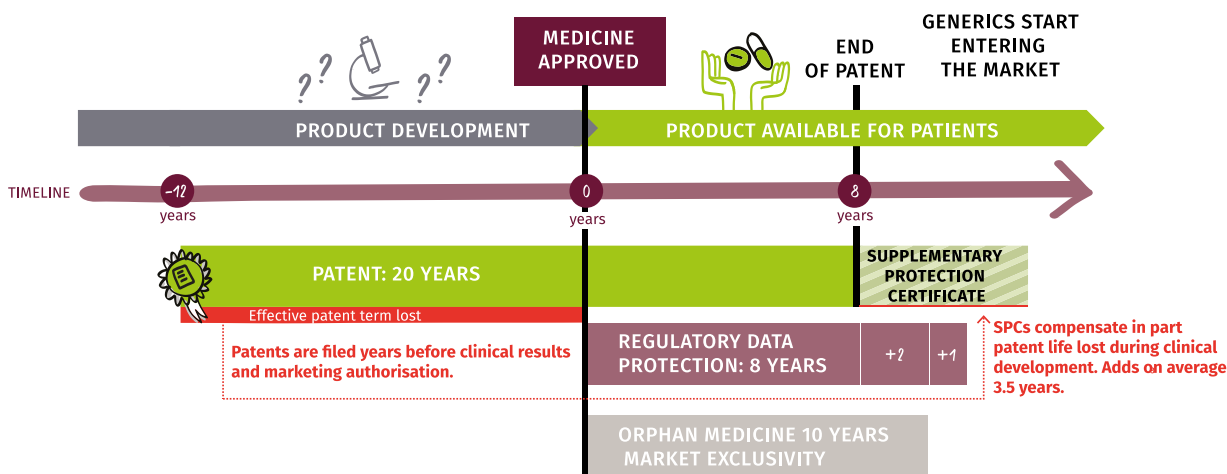
We should also never forget that generic medicines only exist thanks to the R&D investments made by research-based companies. Without patent protection, the business incentive to invest in innovative R&D is muted, and the follow-on generic industry will also have less to copy.

THE AVERAGE EFFECTIVE PROTECTION PERIOD HAS DECREASED BY ABOUT TWO YEARS FROM 15 TO 13 YEARS SINCE 1996

Copenhagen Economics Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe. May 2018

NO PATENTS, NO MEDICINES, INCLUDING GENERICS...

DIFFERENT TYPES OF INCENTIVES ARE REQUIRED TO DRIVE INNOVATION FOR DIFFERENT PATIENTS



¹ MSD Corporate Responsibility Report 2017/2018. Available at <https://www.msdrresponsibility.com/access-to-health/research-development/>
² PwC/strategy&, “The 2018 Global Innovation 1000 study.”



Pharmaceutical incentives provide limited protection from unfair competition. This protection allows biopharmaceutical innovators to continue to invest in future treatments and turn science into valuable medicines for patients.

Incentives provide certainty for companies, which invest in researching and developing new medicines. Thanks to this limited exclusivity, if a medicine makes it to the market, it will be protected from competition for a limited period of time from companies that do not invest in R&D.

Before we can talk about access to medicines, we need to think about the conditions and policies that turn science into new medicines.

PATENTS	<ul style="list-style-type: none"> • 20-year exclusivity term • Filed years before regulatory approval • Publication of the invention 18 months after application 	Publication ensures that other inventors can benefit from state of the art and push their research further !
SUPPLEMENTARY PROTECTION CERTIFICATE	<ul style="list-style-type: none"> • From 0 to 5 years • Total exclusivity of patent + SPC capped at maximum 15 years after regulatory approval 	Average duration of protection for all granted SPCs is 3.5 years. !
REGULATORY DATA PROTECTION	<ul style="list-style-type: none"> • 8 years of data exclusivity (generic companies can't rely on clinical data for EMA approval) +2 years of market exclusivity (no generic on the market) +1 year if new indication is developed • Protects investment to generate pre-clinical and clinical data required for regulatory approval 	Often overlaps with the patent or SPC term and rarely lasts beyond !
ORPHAN DESIGNATION	<ul style="list-style-type: none"> • 10-year market exclusivity linked to one specific orphan designation • Incentivise companies to research and develop medicines for rare diseases 	Market exclusivity does not prevent similar products to be authorised if they demonstrate significant benefit !
PAEDIATRIC EXTENSION	<ul style="list-style-type: none"> • 6-month SPC extension or 2-year extension of orphan market exclusivity • Incentivise companies to do clinical trials to test safety and efficacy of a medicine for children 	Completion of a Paediatric Investigation Plan is agreed with EMA !

WE FIND THAT FOR 51 % OF THE 558 MEDICINAL PRODUCTS ACROSS ALL 28 COUNTRIES A PATENT IS THE LAST MEASURE OF PROTECTION TO EXPIRE. FOR THE REMAINING 49% EITHER THE SPC OR ONE OF THE OTHER INCENTIVES AND REWARDS ARE THE LAST MEASURE OF PROTECTION TO EXPIRE.

Copenhagen Economics, “Study on the economic impact of supplementary protection certificates, pharmaceutical incentives and rewards in Europe.” May 2018



FOR A RENEWED REGULATORY AGENDA

Europe should drive an agile, competitive world-class regulatory system that embraces new scientific and technological breakthroughs in order to accelerate access to innovative products and solutions.

We still have a lot to do to improve care options for patients in Europe and globally. Much of the focus has been on improving access for patients at the point of care. But [delivering access for patients begins with the regulatory process.](#)

Regulatory processes are the means by which we translate science into a licenced treatment that a patient in Europe can use.

For that translation to be effective, we need our regulatory system to be anticipating and working with our level of innovation. Like other pharmaceutical companies, MSD is working with regulatory authorities to deliver on our common goal: renewing Europe's global leadership in regulatory science and practice.

THE PACE OF INNOVATION HAS ACCELERATED DRAMATICALLY IN RECENT YEARS AND REGULATORS NEED TO BE READY TO SUPPORT THE DEVELOPMENT OF INCREASINGLY COMPLEX MEDICINES THAT MORE AND MORE DELIVER HEALTHCARE SOLUTIONS BY CONVERGING DIFFERENT TECHNOLOGIES.

European Medicines Agency, Regulatory Science to 2025 Strategic reflection, December 2018.

REAL WORLD
DATA & EVIDENCE

DYNAMIC
REGULATORY
ASSESSMENT

DRUG-DEVICE
COMBINATION
& BIOMARKER
VALIDATION

INNOVATIVE
CLINICAL TRIAL
APPROACHES

THE WAY EUROPE TREATS
EVIDENCE IN THE FUTURE
WILL EITHER ACT AS A BRAKE
OR AS AN ACCELERATOR IN
OUR ABILITY TO BRING NEW
TREATMENTS TO PATIENTS

VALUE OF INNOVATION

If I have seen a little further, it is by standing on the shoulders of giants.

Isaac Newton



VACCINATION IS AN INVESTMENT

Vaccines are considered one of the greatest successes in medical history. They represent the most effective method to prevent infectious diseases, saving millions of people from illness, disability and death each year.

Vaccination is an investment, with broad benefits that accrue across a lifetime.

Life-course vaccination, meaning vaccination given through all phases of life, helps individuals maintain good health through life, but also has the potential for enormous public health and socioeconomic benefits.


IT IS UNACCEPTABLE THAT IN 2017 THERE ARE STILL CHILDREN DYING OF DISEASES THAT SHOULD LONG HAVE BEEN ERADICATED IN EUROPE.

Jean-Claude Juncker, President of the European Commission, State of the Union Address, 13/09/2017


IN THE ABSENCE OF VACCINATION, ABOUT 90% OF INDIVIDUALS WOULD BE INFECTED WITH MEASLES BEFORE THEY REACHED THE AGE OF 10 (6)

DID YOU KNOW THAT


80% of adolescents and adults who contracted measles **had not been vaccinated**²




It takes up to **36 months to produce a vaccine.** Two-thirds of this time is dedicated to quality control³



Immunization prevents between **2 to 3 million deaths** each year⁴



Measles vaccination **reduced deaths by 84%** between 2000 and 2016⁵



1 WHO, Ten threats to global health in 2019
 2 Ammon, A., & Monné, X., "Vaccines, Trust and European Public Health", 2018
 3 IPROVE, "Roadmap on vaccines in Europe – Vaccine manufacturing and quality control", 2016
 4 WHO, 10 facts on immunization, 2018
 5 CDC, Measles Data and Statistics, 2018
 6 WHO Europe Fact Sheet, "Measles in the WHO European Region", July 2016



BENDING THE CURVE OF CANCER

Cancer incidence continues to rise across Europe. In 2012, the burden of cancer was second greatest with more than one in four deaths due to cancer. Cancer care is changing fast in Europe thanks to the launch of new treatments across various cancer types.

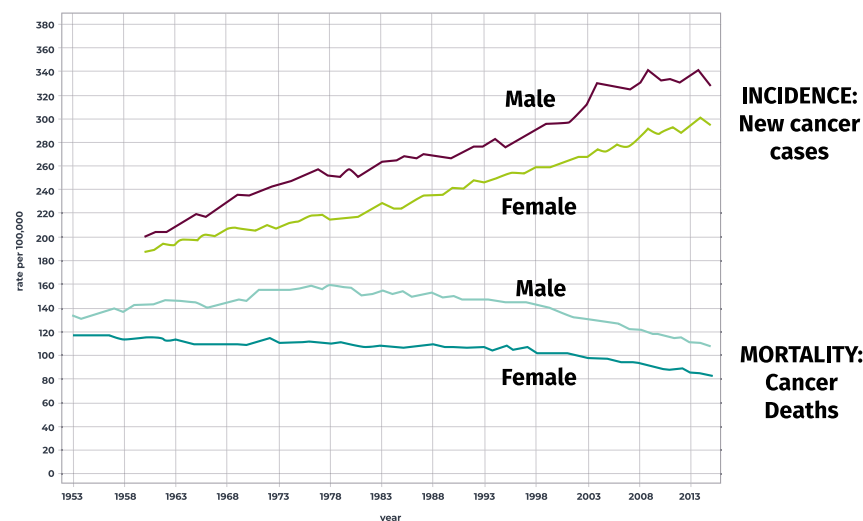
The number of people diagnosed with cancer continues to increase in Europe, up by 30% between 1995 and 2012 due to a growing and aging population.¹

However, advances in diagnostics, medical treatment and screening have helped bring mortality rates down in relative terms. From 2014 to 2018, 57 new molecules with 89 indications were approved.³ Despite this growth and an increased spending on cancer medicines, the overall spending on cancer care has remained stable at around 6% of total health expenditure largely due to a shift towards outpatient care.¹

The number of treatment options continues to increase. In 1996, a physician had only 4 medicines to treat lung cancer. In 2016 there were 19 different medicines available.² The cancer treatment landscape has continued to evolve since 2014, and now includes new medicines targeting 23 different cancer types.³

BENDING THE CURVE OF CANCER

The Impact Of Prevention, Screening, Diagnosis And Treatment¹



Source: NORDCAN© Association of the Nordic Cancer Registries (04/11/2018)

1 Jönsson B et al., "Comparator Report on Patient Access to Cancer Medicines in Europe Revisited", 2016, <http://ihe.se/en/publicering/cancer-medicines-in-europe-2/>
 2 IQVIA Institute, "Global Oncology Trends 2017 – Advances, Complexity, and Costs", May 2017
 3 IQVIA Institute, "Global Oncology Trends 2019 – Therapeutics, Clinical Development and Health System Implications", April 2019



“INNOVATION” IS WHAT HELPS THE PATIENT

Like science, technology progresses through incremental steps. Patients, doctors, and payers all benefit from these innovations through greater choice and competition across and within therapeutic classes.

Everybody likes to talk about “major breakthroughs” and “revolutions”, and critics are quick to downplay “incremental innovation”. But pharmaceutical innovation is first about getting better products that help patients.

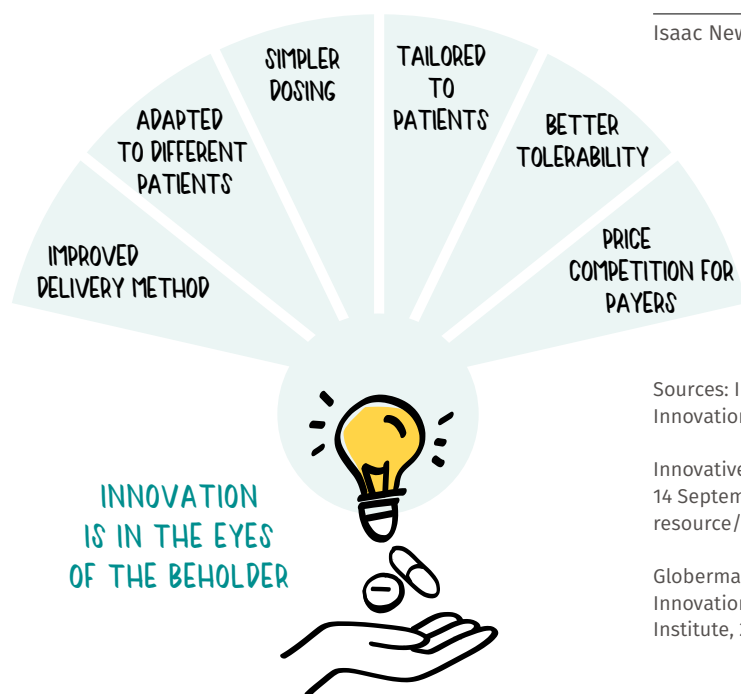
Patients, doctors and payers all benefit from better treatments, be that in the form

of improved drug regimens, less side effects, better tolerability, or ease of use, among others. The patients and their doctors who are helped by these novel treatments welcome such improvements.

The innovation cycle is driven by competition. Companies race in parallel to develop innovative medicines. They strive to come first to market with the best clinical evidence of the value of their medicine. After years of research, new treatments emerge that provide additional clinical data and evidence that have value for the healthcare system, for prescribers, payers and patients.

IF I HAVE SEEN A LITTLE FURTHER IT IS BY STANDING ON THE SHOULDERS OF GIANTS.

Isaac Newton, Letter to Robert Hooke, 1676



Sources: Innovative Medicines Canada, “Incremental Innovation”, 14 September 2016.

Innovative Medicines Canada, “Incremental Innovation”, 14 September 2016. <http://innovativemedicines.ca/resource/incremental-innovation/>

Globerman, S., Lybecker K., “The Benefits of Incremental Innovation: Focus on the Pharmaceutical Industry”, Fraser Institute, 2014.

VALUE FOR MONEY

Innovative medicines and vaccines bring tremendous value for money.

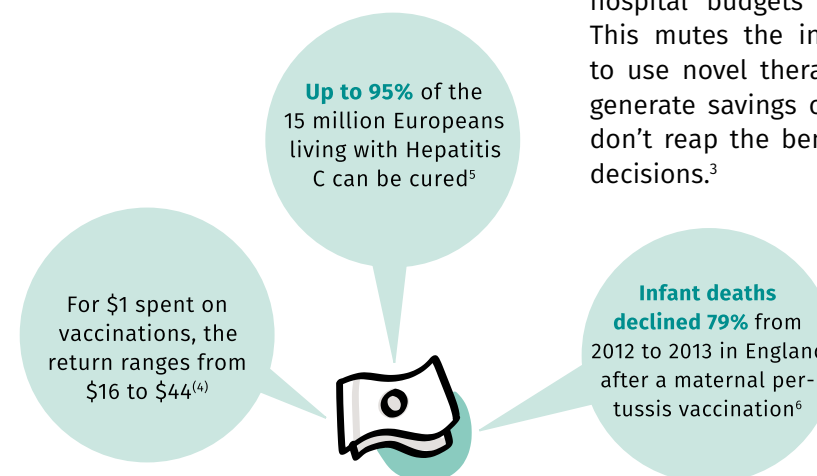
Many more people are alive today and living longer thanks to new medicines and vaccines developed by research-based pharmaceutical companies. More specifically, new treatments bring substantial social and economic contributions to society, generate savings to health systems, and provide new treatment options to patients.¹

Medicines help people avoid disability and death caused by disease and help lower overall healthcare costs.

In fact, medicines have significantly lowered death rates for heart disease, stroke, cancer, and other deadly diseases.²

Healthcare payers and pharmaceutical companies can collaborate in adopting payment models for new products to ensure **fast access for patients** to more effective and safer medicines, **financial predictability** of the drug budget, and **adequate reward** for novel therapies.

Payers also need to ensure that cost savings from hospitalisations are fully credited to improved pharmaceutical spending. In a number of EU countries, medicines and hospital budgets remain fully separated. This mutes the incentive for drug payers to use novel therapies, if by doing so the generate savings outside their budget and don’t reap the benefits of better spending decisions.³



1 IFPMA, “Value of innovation - Discovering Medicines and Vaccines” www.ifpma.org/subtopics/value-of-innovation/

2 Sullivan, T., “The Value of Medicine”, Policy & Medicine, May 2018 www.policymed.com/2010/10/the-value-of-medicine.html

3 Drummond M, Jonsson B., “Moving beyond the drug budget silo mentality in Europe.” Value Health. 2003 doi: 10.1046/j.1524-4733.6.s1.8.x/full; and Espin et al., “Projecting Pharmaceutical Expenditure in EUS to 2021.” 2018

4 Ozawa S., et al., “Return On Investment From Childhood Immunization In Low- And Middle-Income Countries”, Health Affairs Vol. 35, No. 2: Vaccines, Feb. 2016. <https://doi.org/10.1377/hlthaff.2015.1086>

5 EFPIA, “Value of Medicines” <https://www.efpia.eu/about-medicines/use-of-medicines/value-of-medicines/>

6 Amirthalingam G., et al., “Effectiveness of maternal pertussis vaccination in England”, The Lancet, 25 Oct. 2014; 384(9953)



INNOVATING IN ANIMAL HEALTH KEEPS BOTH ANIMALS AND PEOPLE HEALTHY

Ensuring the health of animals is also vital to safeguarding the health of people.

Healthier animals mean a sustainable food supply, protection for humans against diseases passed from animals, and longer, healthier lives for pets. That's why we are committed to the "Science of Healthier Animals".

Disease prevention promotes the health and well-being of both farm and companion animals and prevents suffering. Animal vaccines and other treatments such as parasiticides, not only maintain high standards of animal health and well-being,

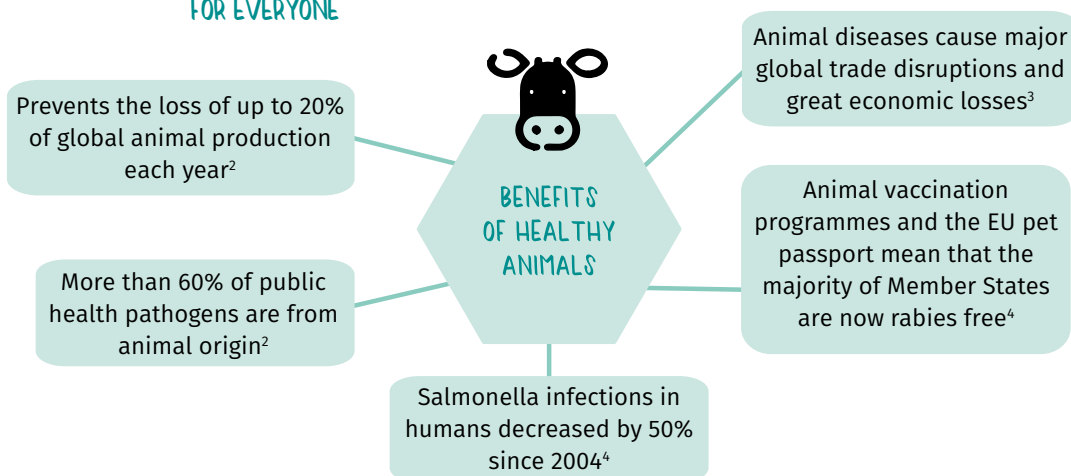
but they also help to protect consumers from harmful food-borne pathogens or zoonotic agents that can come from farm animals.

This holistic approach to health benefits animals, the environment, and people. Animal health experts, veterinarians and farmers work hand in hand for a better health, well-being, and food safety. To promote prevention, 9 million European farmers need continued support from European authorities.

ANIMAL VACCINATION IS NEEDED TO KEEP ANIMALS HEALTHY – AN IMPORTANT PART OF THE “ONE HEALTH” APPROACH. PREVENTION IS BETTER THAN CURE!

Vytenis Andriukaitis, European Commissioner for Public Health, 20 April 2018¹

FROM FARM TO FORK ANIMAL HEALTH MATTERS FOR EVERYONE



¹ https://twitter.com/V_Andriukaitis/status/987260364579594240

² World Organisation for Animal Health, "Deepening the understanding of the economics of animal health to optimise the management of disease threats" 23 May 2016

³ Since the start of the millennium, six international incidents of animal disease caused economic losses of almost €70 billion (<https://www.animalhealthurope.eu/resources/infographics.html#livestockcounts>)

⁴ Animal Health Europe Manifesto <https://www.animalhealthurope.eu/focus-area/91-manifesto-2019.html>

HEALTH COSTS

The health and wealth of a nation are fundamentally linked. Healthier populations live longer, more productive lives, leading to greater economic prosperity.

The Lancet, Editorial, 16 March 2019

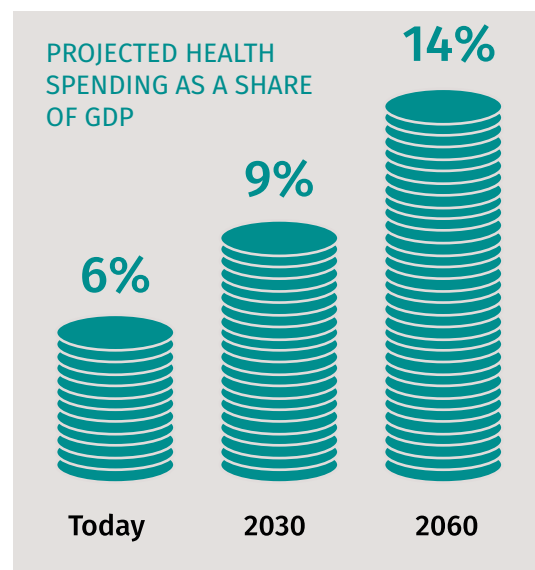


WHY DO HEALTH COSTS INCREASE?

Healthcare costs have been on a rising trajectory for decades. These increases are driven by demographic changes, greater demand for healthcare, and new technologies that treat more diseases. These trends together converge to put greater pressure on budgets.

During the last 50 years, developed countries have seen healthcare expenditures increase at an average rate of 2 percentage points per annum over GDP growth.¹ Based on current trends, the average share of GDP spent by OECD countries would increase to 14% by 2060.²

Healthcare cost increases have primarily been caused by our ability to treat more diseases and rising demand for healthcare services.



The pathway to sustainable healthcare systems requires fundamental changes going beyond a single focus on pharmaceutical spending. Moving towards a value-based approach to healthcare can meet the goal of access to effective and affordable care by addressing inefficiencies and quality issues. The OECD found that *“a significant share of health spending in OECD countries is at best ineffective and at worst, wasteful”*. Based on existing estimates, it found that **one-fifth of health spending could be channelled towards better use** and that cutting ineffective spending and waste could produce significant savings. For the OECD, moving *“towards a more value-based health care system must be pursued decisively”* by policy makers faced with ever-growing health care expenditure.

FINDING POLICIES THAT CAN MAKE HEALTH SPENDING MORE SUSTAINABLE WITHOUT COMPROMISING IMPORTANT ACHIEVEMENTS IN ACCESS AND QUALITY REQUIRES EFFECTIVE CO-OPERATION BETWEEN HEALTH AND FINANCE MINISTRIES.

OECD in Fiscal Sustainability of Health Systems

1 World Economic Forum, McKinsey, “The Financial Sustainability of Health Systems – A Case for Change”, 2012

2 OECD, “Fiscal Sustainability of Health Systems – Bridging Health and Finance Perspectives”, 2015



DISEASE IS THE REAL COST

Disease is the real cost to society, not the treatment. Every person who is absent from work or has lower productivity represents an economic loss to society. In 2008 premature cancer-related deaths in Europe resulted in lost productivity costs amounting to €75 billion.¹ In Germany alone, the cost of illness was estimated at €338.2 billion in 2015.²

THE COST OF DISEASE COULD BANKRUPT HEALTHCARE SYSTEMS WITHOUT NEW MEDICINES

Andy Powrie-Smith, EFPIA, Medicines costs in context.⁴

TODAY, CLOSE TO 30 DISEASES ARE PREVENTABLE BY VACCINATION PREVENTING BETWEEN 2 AND 3 MILLION DEATHS GLOBALLY PER YEAR

Source: 10 facts on immunization, WHO

Fiscal policy should integrate the value of treating disease as a key component of achieving macro-economic objectives.³ Innovative medicines can put healthcare systems on a more sustainable path by reducing costs in other parts of the healthcare system such as hospitalisations and clinicians’ time.⁵

To illustrate, the OECD has estimated the total costs related to mental ill-health at more than 4% of GDP – or over €600 billion – across the 28 EU countries in 2015. €190 billion represents direct spending on health care, another €170 billion is spending on social security programmes, while a further €40 billion is caused by indirect costs in the labour market – driven by lower employment rates and reduced productivity due to mental illness.⁶



1 Hanly, P., Soerjomataram, I., & Sharp, L. (2015). “Measuring the societal burden of cancer: The cost of loss productivity due to premature cancer-related mortality in Europe.” *Int. Journal of Cancer*, 136-145.

2 Statistisches Bundesamt (Destatis). (2017, September 29). Charts. Retrieved from Cost of illness: <https://www.destatis.de/EN/FactsFigures/SocietyState/Health/CostIllness/CostIllness.html>

3 Rheinberger, C., Herrera-Araujo, D., & Hammit, J. (2016). “The value of disease prevention vs treatment.” *Journal of Health Economics*, 247-255.

4 Medicines costs in context. Retrieved from Value of medicines: <https://www.efpia.eu/about-medicines/use-of-medicines/value-of-medicines/>

5 Kumar, V., & Sundarraj, R. (2018). *The Societal Value of Pharmaceutical Innovation*. Global Innovation and Economic Value (pp. 147-187). New Delhi: Springer.

6 OECD/EU Health at a Glance: Europe 2018



HEAVY FOCUS ON DRUG BUDGETS

Governments have been targeting drug expenditures as their main opportunity to achieve savings.

Many European governments have accelerated the implementation of cost-containment measures in their healthcare systems as a response to the financial and fiscal crisis. Their primary target for cost-cutting has been pharmaceutical expenditures. As a result, pharmaceutical spending is no longer

the primary driver of increased healthcare spending.¹

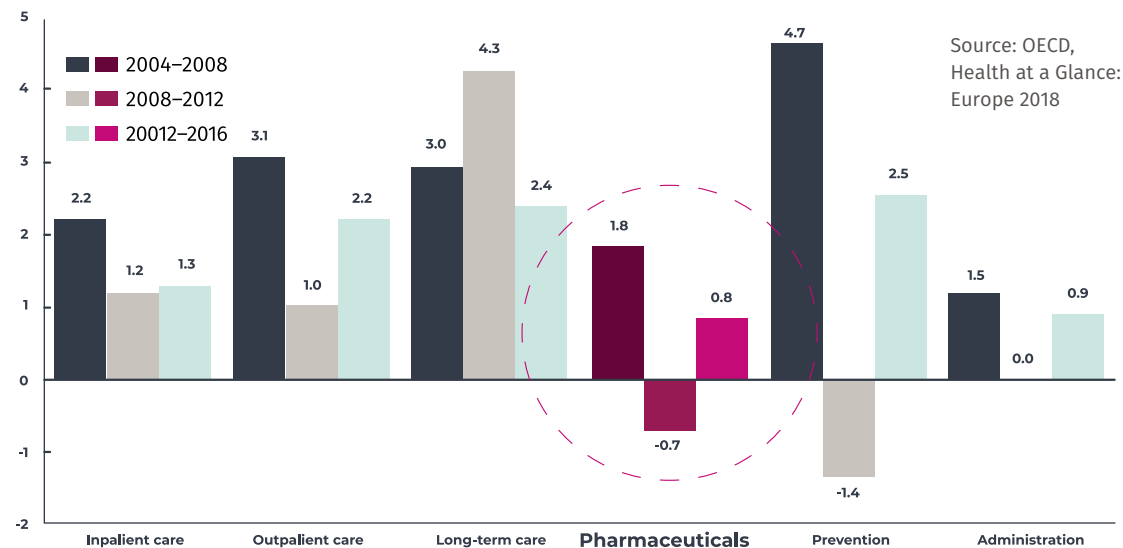
According to the International Monetary Fund, the focus of cost-containment efforts on pharmaceuticals in Europe *“are unlikely to have a major effect on the growth of spending over the longer term, especially given the modest share of pharmaceutical outlays in total public health outlays (about 15 percent in the OECD countries)”*.²

AFTER THE FINANCIAL CRISIS, EU RETAIL PHARMACEUTICAL EXPENDITURE FELL BY AN ANNUAL AVERAGE RATE OF 0.7% BETWEEN 2008 AND 2012. SPENDING THEN RECOVERED BETWEEN 2012 AND 2016, RISING BY AN AVERAGE OF 0.8% PER YEAR.

OECD/EU (2018), Health at a Glance: Europe 2018: State of Health in the EU Cycle, OECD Publishing, Paris.

GROWTH OF HEALTH SPENDING PER CAPITA FOR SELECTED FUNCTIONS

EU average, 2004–16



¹ OECD/EU Health at a Glance: Europe 2018

² International Monetary Fund, Fiscal Monitor, “Fiscal Exit: From Strategy to Implementation”, Nov. 2010, page 56.

PENNY WISE, EURO FOOLISH

Despite representing about a sixth of healthcare spending, the pharmaceutical budget remains disproportionately targeted at cost-cutting. During the last decade, health cost increases have actually been driven primarily by other types of healthcare spending (hospitalisation, etc.). However, short-term budget savings can come at a long-term cost.

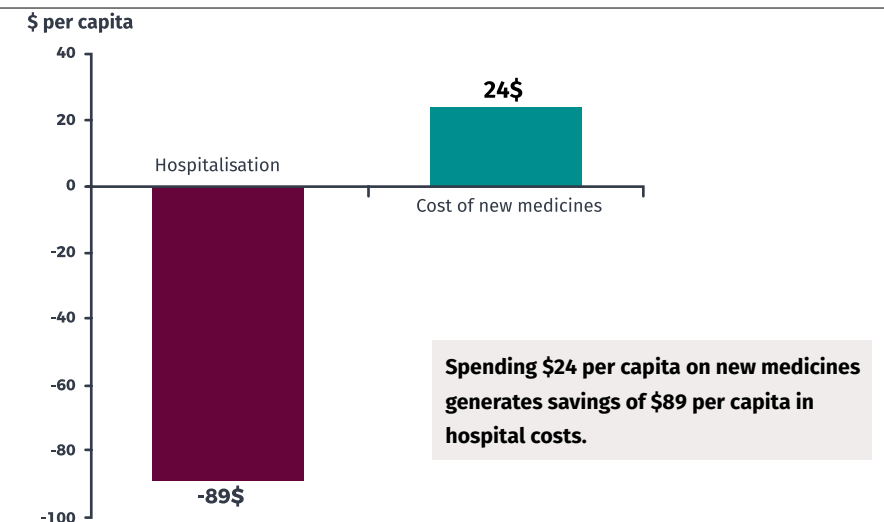
Appropriate use of innovative medicines can reduce patient costs being shifted to more expensive areas such as hospitalisation, and clinicians’ time. Prescription medicines are largely responsible for the on-going shift away from hospitalisation and toward more affordable patient care.

When access to innovative medicines is slowed down, healthcare systems lose out on potentially greater savings, but more importantly on better health outcomes!¹

ALTHOUGH NEW DRUGS CAN APPEAR EXPENSIVE WHEN CONSIDERED IN ISOLATION, PHARMACEUTICAL INNOVATION LEADS TO COST SAVINGS ELSEWHERE IN THE SYSTEM THROUGH THE REDUCED USE OF HEALTH SERVICES LIKE HOSPITALS AND NURSING HOMES

Prof. Frank R. Lichtenberg, Columbia University Graduate School of Business

IMPACT ON HOSPITALISATION COST OF USE OF NEW CARDIOVASCULAR TREATMENTS (1995-2004)



Frank R. Lichtenberg, 2009. “Have newer cardiovascular drugs reduced hospitalization? Evidence from longitudinal country level data on 20 OECD countries, 1995-2003.” Health Economics, John Wiley & Sons, Ltd., vol. 18(5), pages 519–534.

¹ IPHA, “New Medicines for Patients as Fast as in Europe: Need for Sustained Funding Growth”, 2018



PHARMACEUTICAL EXPENDITURES

Pharmaceuticals play a vital role in the health system.

OECD, Health at a Glance, EU 2018

GROWTH OF DRUG SPENDING

During the last decade, pharmaceutical prices have not been the driver of increased healthcare costs.

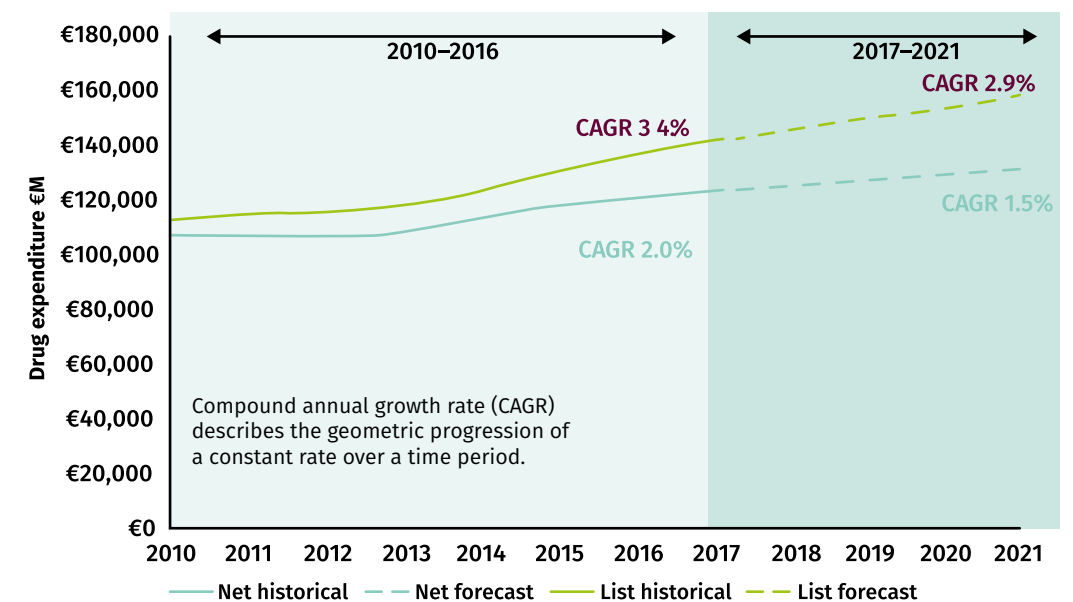
Since 2005, pharmaceutical spending has been outpaced by the growth of total health expenditures. The economic crisis accelerated this trend and “had a significant effect on pharmaceutical spending in many OECD countries” (OECD 2018). A number of European countries, in particular, experienced a downward reversal in pharmaceutical spending trends pre- and post-crisis.

A recent analysis by Espin et al. shows that in the EU5¹ pharmaceutical net expenditure is expected to grow at a sustainable yearly rate of 1.5%, in other words at the same rate as the forecast GDP growth.

OUR RESULTS SUGGEST THAT PHARMACEUTICAL EXPENDITURE IS UNDER CONTROL, BELOW PREDICTED HEALTHCARE EXPENDITURE GROWTH IN EUROPE, AND IN LINE WITH LONG-TERM ECONOMIC GROWTH RATES.

Espin et al., 2018

HISTORICAL AND FORECAST DRUG EXPENDITURE IN FRANCE, GERMANY, ITALY, SPAIN, AND THE UK



Source: Espin et al., “Projecting Pharmaceutical Expenditure in EUS to 2021: Adjusting for the Impact of Discounts and Rebates.” Applied Health Economics and Health Policy, 2018

¹ “EU5” refers to France, Germany, Italy, Spain, and the UK.



SO HOW MUCH DO WE SPEND ON PHARMACEUTICALS IN THE EU?

According to the OECD, in 2016, European citizens spent EUR 417 per capita on retail pharmaceuticals.¹

However, this number is only part of the story. On the one hand, due to national reporting differences, it doesn't cover all the spending on pharmaceuticals used in hospitals, "which can typically add another 20% to a country's pharmaceutical bill." (OECD/EU, Health at a Glance, 2018).

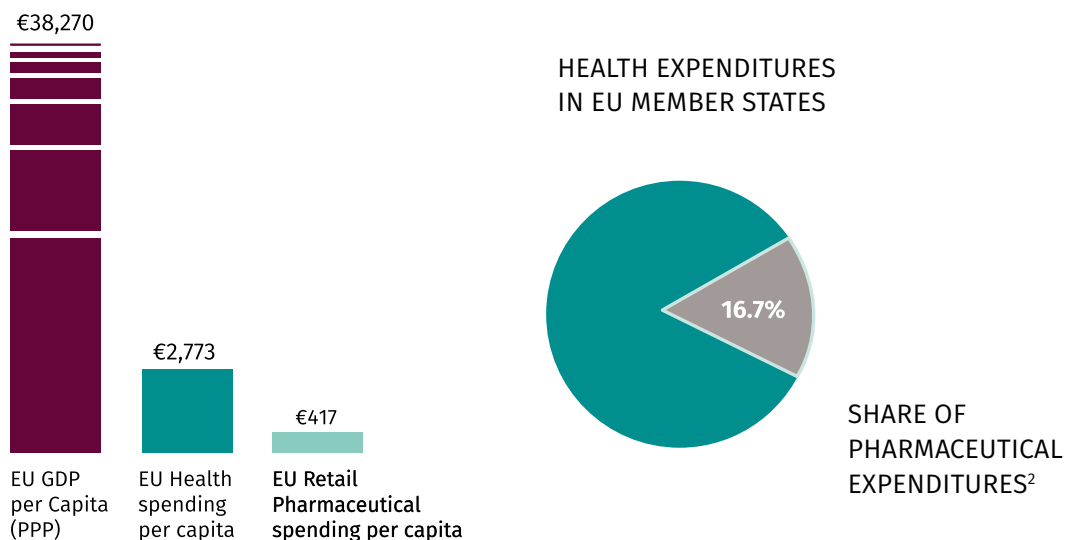
On the other hand, only "around four out of every five euros spent on retail pharmaceuticals goes on prescription medicines, with the rest on over-the-counter medicines." (OECD 2018).

PHARMACEUTICALS PLAY A VITAL ROLE IN THE HEALTH SYSTEM. AFTER INPATIENT AND OUTPATIENT CARE, PHARMACEUTICALS (EXCLUDING THOSE USED IN HOSPITALS) REPRESENT ONLY THE THIRD LARGEST ITEM OF HEALTH CARE SPENDING, ACCOUNTING FOR A SIXTH OF HEALTH EXPENDITURE IN THE EU IN 2016.

OECD/EU, Health at a Glance 2018

PUTTING PHARMACEUTICAL EXPENDITURES IN PERSPECTIVE

EUROSTAT, OECD/EU Health at a Glance, 2018, Adjusted for Purchasing Power Parity



1 Pharmaceutical expenditure per capita is adjusted to take account of differences in purchasing power.
 2 WHO EUROPE, Total pharmaceutical expenditure as percentage of total health expenditure, Accessed 29 June 2019. https://gateway.euro.who.int/en/indicators/hfa_578-6770-total-pharmaceutical-expenditure-as-of-total-health-expenditure/visualizations/#id=19673&tab=table



THE "PUBLIC" PRICE IS NOT WHAT THE PUBLIC PAYS

When talking about pharmaceutical prices, people generally refer to the public price of a medicine. This is understandable as it is often the only known "official price". In fact, the actual price of a new medicine is set through a long negotiation process by which the actual, final, and "net price" paid by the purchaser is set.

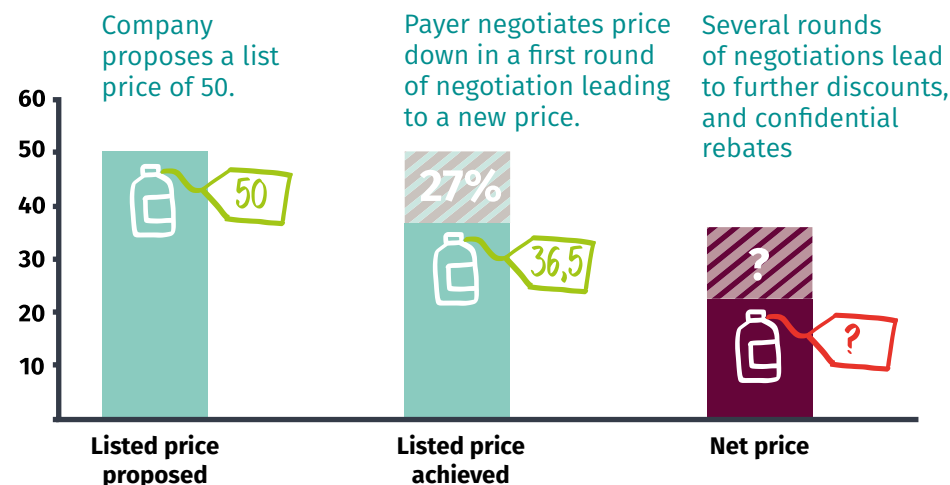
This "net price" is set through price control regulations, international price comparisons, cost-effectiveness reviews, confidential rebates and sometimes budget caps that require companies to reimburse payers above a certain volume. As a result of this lengthy process and negotiations, the "public price" that one may read about in the papers, including in academic journals, is hardly ever the real price paid by health systems.

In the EU, most healthcare systems benefit from strong negotiation power as sole purchasers or decision makers on the reimbursement level of pharmaceuticals.

Public payers have been using this power and have developed a number of cost-containment measures that are intended to keep their pharmaceutical budgets in check. Some of these measures target indiscriminately across all types of pharmaceutical spending and potentially impact innovative companies and their ability to re-invest their revenues into R&D.

At MSD, we engage actively with payers to find the appropriate and flexible solutions that take into account budget considerations, access for patients, and appropriate reward for new treatments.

SIMPLIFIED PRICE NEGOTIATION TO ILLUSTRATE PRICE SETTING IN SOME EUROPEAN COUNTRIES





INTERNATIONAL PRICE COMPARISON

Can we sustain affordability of drugs across Europe if countries with very different GDP per capita, different levels of healthcare spending, different epidemiology, and different public health priorities, want the same price?

Comparing pharmaceutical prices between different countries is called “external reference pricing”. It is widely used across Europe. It is the process by which national payers include the price paid by other countries in their own pricing calculation for medicines. It may include a few neighbouring countries or all EU countries using the lowest price or lowest average from a selection of countries.

The most detrimental effect of external reference pricing is that it may result in price convergence across countries that do

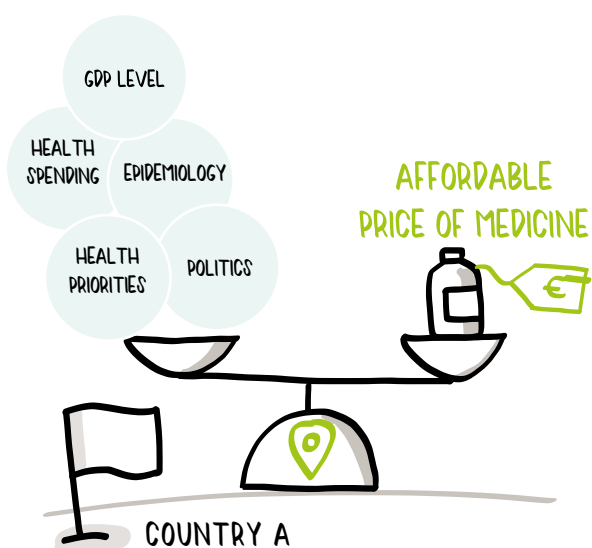
not have the same level of GDP, spending levels on healthcare, or health priorities. Price convergence prevents from adjusting the price to a particular country’s health priorities or ability to pay (given its potential impact on other countries’ prices).

As a result, external reference pricing may cause slower access to innovative drugs in low income countries, and greater uncertainty for companies wishing to increase access to their products across the EU.

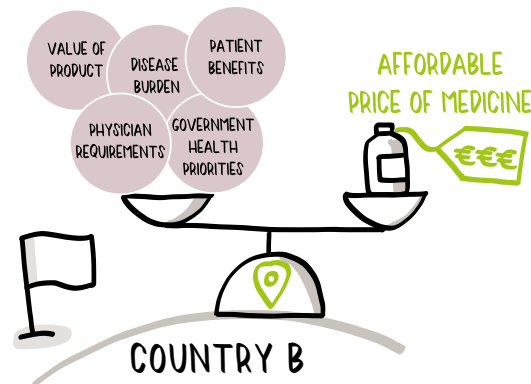
In order to improve affordability, MSD suggests that prices of medicines be based on a variety of criteria, including: the value of the product, patient benefits, the disease burden, government health priorities and physician requirements.

PRICING TO MARKET IS INCREASINGLY NOT POSSIBLE IN AN ERA OF FREE TRADE AND EXTERNAL PRICE REFERENCING. THIS MAY WELL RESULT IN PROBLEMS IN THE AVAILABILITY AND AFFORDABILITY OF SOME MEDICINES IN SOME COUNTRIES

OECD Report “Pharmaceutical Pricing Policies in a Global Market”, 2008



PRICE COMPARISONS ACROSS COUNTRIES PREVENT DIFFERENTIAL PRICING THAT IS ADJUSTED TO THE SPECIFIC NEEDS AND ABILITY TO PAY FOR LOW-INCOME COUNTRIES



COUNTRY B



PHARMACEUTICAL PRICE TRANSPARENCY IN THE SPOTLIGHT

While confidential rebates lower the prices paid by health systems, stakeholders are calling for more transparency in price setting.

At the core of the argument for greater transparency of net prices is the concern that one country may pay more than its neighbour. But what if the neighbour is not so affluent and its ability to pay is much lower? Should the more affluent country benefit from the same price?

Price transparency may thus undermine so-called differential pricing, i.e. the ability of companies to adjust their prices at a level more in line with the particular needs and ability to pay of a lower income country.¹

Economists argue that confidential net prices help achieve maximum access and optimal allocation of resources.³ This is common across industries, including other areas of healthcare. If lower income Member States disclose the prices they pay after confidential rebates, this will deter companies from providing them deeper discounts and impact affordability.³

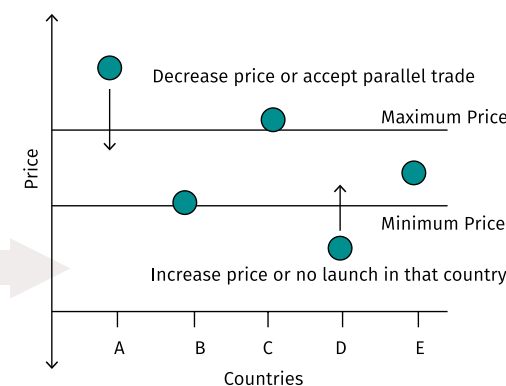
Price transparency may also restrict competition and lead to more uniform pricing across Europe, which will not necessarily benefit patients in lower income countries.⁴

A SIMILAR PRICE-LEVEL LEADS TO A DIFFERENT LEVEL OF AFFORDABILITY DEPENDING ON THE ECONOMIC SITUATION OF EACH COUNTRY. ATTENTION COULD BE GIVEN TO MEASURES THAT ALLOW COMPANIES TO OFFER MEDICINES AT AFFORDABLE PRICES IN EACH EU COUNTRY

High Level Pharmaceutical Forum 2005-2008 Final Report 2008

IMPACT OF PRICE TRANSPARENCY AND PARALLEL TRADE: A NARROWER PRICE CORRIDOR FOR PRICING IN EUROPE²

EFFICIENT PRICING REQUIRES THAT DIFFERENT CUSTOMERS ARE CHARGED DIFFERENT AMOUNTS, ACCORDING TO THEIR DIFFERENT NEEDS AND VALUATIONS¹



1 Dermot Glynn, “The case for transparency in pricing”, Europe Economics, 2016
 2 Zoltan Kalo, “Differential Pricing across Europe - Addressing CEE Countries Needs”, ISPOR, 10 Nov. 2014
 3 Danzon PM, Towse A., “Differential pricing for pharmaceuticals: reconciling access, R&D and patents”, Int J Health Care Finance Econ. 3 Sept.2003, 183-205.
 4 The European Commission identified this risk in its Final Report of the Pharmaceutical Sector Inquiry when discussing price transparency in the context of tendering procedures. See paragraph 1485 of the Final report adopted in July 2009.



REWARD VALUE TO THE PATIENT

Pricing and reimbursement systems should be based on patients' health outcomes, promote rapid access, reward innovation, and be predictable and transparent.

After marketing approval, pricing & reimbursement is a crucial step in ensuring that patients have access to innovative medicines.

At MSD we are constantly engaged with payers to ensure we reach our common goals of improved health outcomes and sustainable budgets.

We strive to achieve mutually beneficial agreements with payers to ensure that our medicines and vaccines are accessible and affordable, while ensuring that we can continue to invest in the next generation of MSD inventions.

IN EUROPE, [PRICING DECISIONS] REMAIN UNPREDICTABLE. [...] THIS RESULTS IN AN UNPREDICTABLE LOTTERY FOR COMPANIES WHO HAVE BROUGHT A PRODUCT THROUGH A SERIES OF REGULATORY HURDLES AND STILL DO NOT KNOW WHAT THE FINAL REIMBURSEMENT PRICE WILL BE.

WHO Report "Priority Medicines for Europe and the World", 2004



SPECIAL CHALLENGES

There is learning in failure. And while those setbacks can be disheartening, they are worth it because when we do succeed it can save lives.

Kenneth Frazier
Chairman & CEO, MSD



ANTIMICROBIAL RESISTANCE A GLOBAL THREAT TO HEALTH

New collaborations and incentives are needed to revitalise research and development of new antibiotics

Antibiotics have revolutionised infectious disease treatment, saving millions of lives worldwide. However, **rising levels of resistance to antibiotics are reducing the effectiveness of these treatments and putting these health gains at risk.**

Every year at least 25,000 people in the EU alone die from infections caused by resistant bacteria. Unless action is taken, we could revert to a world where simple infections are no longer treatable. Rising levels of resistance to antimicrobials have become a serious threat to global health security and economic growth.

Antimicrobial resistance (AMR) results from the ability of micro-organisms to resist antimicrobial treatments - including antibiotics. AMR has a direct impact on human and animal health and carries a heavy economic burden due to longer hospital stays, higher medical costs and increased mortality. New antibiotics are urgently needed to address the growing threat of resistance; however, there are relatively few in development.¹ Antibiotic research and development present unique scientific, regulatory, and economic challenges.

The EU and Member State governments can address these barriers and revitalise R&D in this area through implementation of a suite of push and pull incentives to support antimicrobial innovation and appropriate use.

For more than 80 years, MSD has played a significant role in the discovery and development of novel medicines and vaccines to treat and prevent infectious diseases. Today, **MSD is one of only a few large pharmaceutical companies that sustains its R&D investments on developing vaccines and medicines to prevent and treat bacterial infections.**

Beyond R&D, we are making significant investments into tools and services to support appropriate use of antimicrobials. These include SMART – one of the world's largest AMR surveillance initiatives, antimicrobial stewardship partnerships with hospitals around the world, and programmes working with farmers to scale up the use of vaccination that helps optimise the use of antimicrobials in animals.²

AS OF MAY 2017, 51 ANTIBIOTICS AND 11 BIOLOGICALS WERE IN THE CLINICAL PIPELINE. ONLY 5 ARE EXPECTED TO REACH THE MARKET³

¹ IFPMA members' antibacterial compounds pipeline inventory 2015 (<https://www.ifpma.org/resource-centre/ifpma-infographic-ifpma-members-antibacterial-compounds-pipeline-inventory-2015/>)

² "SMART" stands for the Study for Monitoring Antimicrobial Resistance Trends. For more information, please go to <http://www.globalSMARTsite.com/>

³ DRIVE-AB Report, "Revitalizing the antibiotic pipeline", 2018 (<http://drive-ab.eu/wp-content/uploads/2018/01/DRIVE-ABExecutive-Summary-Jan2018.pdf>)



AS OF DECEMBER 2017 MSD HAS:

5 Compounds in late-stage development for the potential treatment or prevention of infectious diseases

20 Ongoing Phase 2/Phase 3 clinical trials evaluating compounds addressing infectious diseases

THE EFFECTIVE STIMULATION OF ANTIBIOTIC INNOVATION REQUIRES A BALANCED COMBINATION OF BOTH "PUSH" INCENTIVES (THOSE THAT SUPPORT R&D DIRECTLY) AND "PULL" INCENTIVES (THOSE THAT REWARD NEW PRODUCTS).

Innovative Medicines Initiative DRIVE-AB report on "Revitalizing the antibiotic pipeline – Stimulating innovation while driving sustainable use and global access"



SCIENTIFIC CHALLENGES

- ! Constantly evolving bacteria
- ! Resistance difficult to predict

PUSH INCENTIVES

Reduce the risk of early investment in antibiotic R&D

Incentives such as grants and refundable tax credits can stimulate pre-clinical and clinical R&D.



REGULATORY CHALLENGES

- ! Complex clinical trials
- ! Complex regulatory pathways

DELINKED MECHANISMS

Reward innovation earlier in a product's life cycle when use is low

Incentives such as market entry rewards and transferable exclusivity partially delink the expected economic return to sales volume early in the product life cycle. These could address a key challenge for novel antibiotics.



ECONOMIC CHALLENGES

- ! Novel antibiotics generally undervalued by reimbursement and HTA systems
- ! Uptake of novel antibiotics slow as used sparingly to preserve effectiveness
- ! Reimbursement systems discourage the appropriate use of novel antibiotics

PAYMENT & HTA REFORM

Enable access to novel antibiotics and stabilise the economics of antibiotic R&D

Bundled payment mechanisms that apply in hospitals discourage appropriate use of novel antibiotics. New approaches in Health Technology Assessment are also needed to capture the societal value of novel antibiotics.

Source: MSD Antimicrobial Resistance Global Action Plan <https://www.msdrresponsibility.com/access-to-health/infectious-diseases/antimicrobialsantibiotics/>



PATIENT ACCESS DELAYS

Despite a marketing approval granted by the European Commission, patients are not equal when it comes to getting access to innovative medicines in the EU. The time between the EU market approval and the pricing/reimbursement decision varies from from 119 to 925 days.

In December 2018, depending on the patients' country of residence, doctors could prescribe between 14% and 85% of a sample of 121 new medicines approved in the EU between 1 January 2015 and 31 December 2017. Patient access to new medicines is highly varied across Europe. The average delay between market authorisation and patient access can

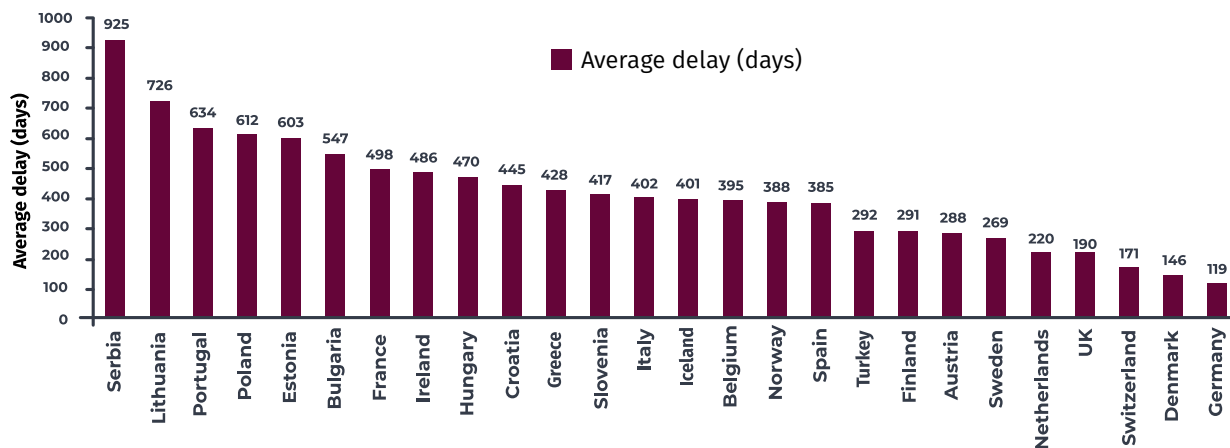
vary by a factor greater than x 7 across Europe, with patients in Northern/Western Europe accessing new products 100-200 days after market authorisation and patients mainly in Southern/Eastern Europe between 600-1000 days.

DELAYED PRICING AND REIMBURSEMENT DECISIONS DEFER THE AVAILABILITY OF MEDICINES. SUCH DELAYS AFFECT PATIENTS AND RESEARCH-BASED COMPANIES.

EU Commission Press Release March 2012

AVERAGE TIME BETWEEN MARKETING AUTHORISATION AND PATIENT ACCESS

IQVIA 2018 study: 2015 to 2017



For most countries patient access equates to granting of the reimbursement list, except for hospital products in Finland, Norway and Sweden, where some products are not covered by the general reimbursement scheme and so zero-delay is artificially declining the median and average. In France, delays may be shorter for some innovative treatments thanks to the Autorisation Temporaire d'Utilisation.

Source: EFPIA Patient W.A.I.T. Indicator Survey 2018. April 2019. <https://www.efpia.eu/media/412747/efpia-patient-wait-indicator-study-2018-results-030419.pdf>

ORPHAN MEDICINES FOR MILLIONS OF EU CITIZENS

Orphan medicines address rare diseases that affect no more than 1 in 2,000 people (or 5 in 10,000). In Europe, approximately 30 million people live with a rare disease.¹

Since the introduction of the EU Orphan Medicine Regulation in 2000 and the 10-year exclusivity it grants to innovators,² we have seen tremendous growth in rare disease innovation leading to over 160 new treatments. EU orphan incentives are working and are necessary to sustain R&D in rare diseases.

Despite the tremendous success so far, there is still high unmet medical need in rare diseases: only 5% of rare diseases have an approved treatment and much work remains to be done.³

The growth in public and private investment in rare disease R&D resulting from the introduction of the EU Orphan Medicine Regulation has had a considerable impact on innovation and patient outcomes.⁴ Maintaining the right regulatory, scientific and economic environment for orphan medicine development is critical in giving hope to patient.

SINCE YEAR 2000⁵

 **2,121** ORPHAN DESIGNATIONS

 **164** ORPHAN MEDICINES AUTHORISED

THE EU REGULATION ON ORPHAN MEDICINAL PRODUCTS CONTINUES TO BE A SUCCESS IN FULFILLING ITS PRIMARY PURPOSE - TO ATTRACT INVESTMENT TO THE DEVELOPMENT OF THERAPIES FOR LIFE-THREATENING OR DEBILITATING DISEASES FOR MILLIONS OF PEOPLE WHO TODAY HAVE EITHER NO TREATMENT AT ALL OR NO SATISFACTORY TREATMENT.

EURORDIS Rare Disease Europe, "Breaking the Access Deadlock to Leave No One Behind", January 2018.

1 EMA, Orphan designation: Overview, 2019

2 Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.

3 Global Genes, Rare Facts, <https://globalgenes.org/rare-facts>

4 Kesselheim A, Avorn J., "The most transformative drugs of the past 25 years: a survey of physicians", Nature Reviews Drug Discovery 12; 425-431, 2013

5 European Medicines Agency, "Annual report on the use of the special contribution for orphan medicinal products", January 2019.



HEALTH TECHNOLOGY ASSESSMENT

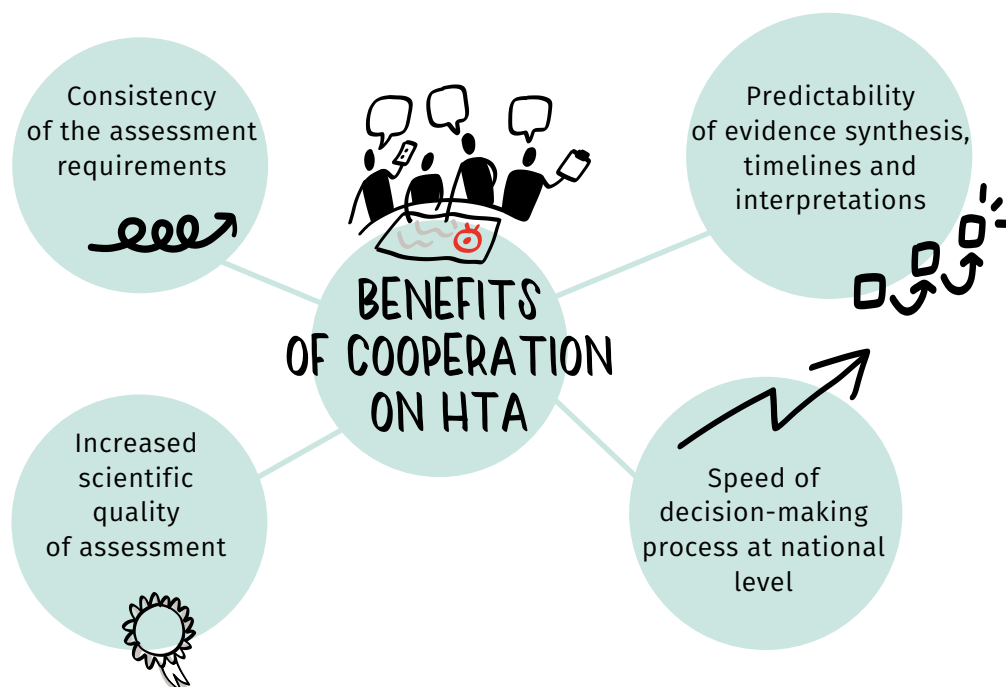
Health Technology Assessment (HTA) is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, and robust manner.

HTAs are conducted at the national level, but the EU is working toward harmonisation of HTA requirements for efficacy assessments and the early generation of real-world data to inform EU regulatory decisions and HTA, pricing, and reimbursement decisions for products. We support HTA assessments conducted using sound scientific methods.

It is crucial that both private and public bodies that produce or review the evidence follow agreed upon, scientifically validated and transparent methodologies. HTAs can be an important process through which the value of a medicine or vaccine can be investigated in the context of a set population's needs.

Harmonisation of HTA requirements for efficacy assessments is critical for patients to avoid duplicative work, such as unnecessary trials, potential delays, and access restrictions that are not based on the intrinsic properties of a medicine, but administrative requirements.

WHEN HTAS ARE TRANSPARENT, UNBIASED, AND FIRMLY ROOTED IN RESEARCH AND THE SCIENTIFIC METHOD, THEY ARE A POWERFUL TOOL TO ENCOURAGE AND REWARD INNOVATION WITH THE GREATEST VALUE TO PATIENTS AND SOCIETY



BEYOND INNOVATION

As we strive to achieve the Sustainable Development Goals, it is clear that we need more innovative collaboration among government, civil society, and the business community to deliver stronger results for people around the world.

Dr. Mary-Ann Etiebet, Lead and Executive Director at MSD for Mothers



MSD FOR MOTHERS

Globally, every two minutes, a woman dies from complications related to pregnancy and childbirth. Most of these deaths are preventable when women have access to modern contraception and quality maternal healthcare before, during, and after childbirth.

In 2011, MSD launched “MSD for Mothers”, a 10-year, \$500 million initiative to reduce maternal mortality worldwide. Today, MSD is working with more than 100 partners in 48 countries to improve maternal health.

Our efforts target three areas:

- **Enable health providers** by providing the skills, tools and technologies they need
- **Develop and deliver life-saving products** for women and their health providers.
- **Empower women** to make informed choices about contraception and get the quality care they need for a healthy pregnancy and safe childbirth.



IN THE SUCCESSFUL COOPERATION WITH MSD FOR MOTHERS, MATERNAL MORTALITY IS PUT IN FOCUS. ACCESS TO MATERNAL HEALTHCARE IS A FUNDAMENTAL HUMAN RIGHT. IT IS A JOINT RESPONSIBILITY OF DECISION MAKERS IN POLITICS AS WELL AS THE PRIVATE SECTOR TO WORK TOWARDS ENDING MATERNAL MORTALITY.

Silvana Koch-Mehrin, Founder and President of Women Political Leaders Global Forum



6.6 MILLION WOMEN REACHED AND COUNTING

16 EUROPEAN COUNTRIES WITH MSD FOR MOTHERS INITIATIVES

HER LIFE

2.5m women with improved quality of care

3.7m women with access to modern contraception

638k women empowered to demand quality care

HER HEALTHCARE

51k providers equipped to offer quality care

18.9m people with access to quality facilities

15.4m people with access to lifesaving medicines

NOBODY LEFT OUTSIDE

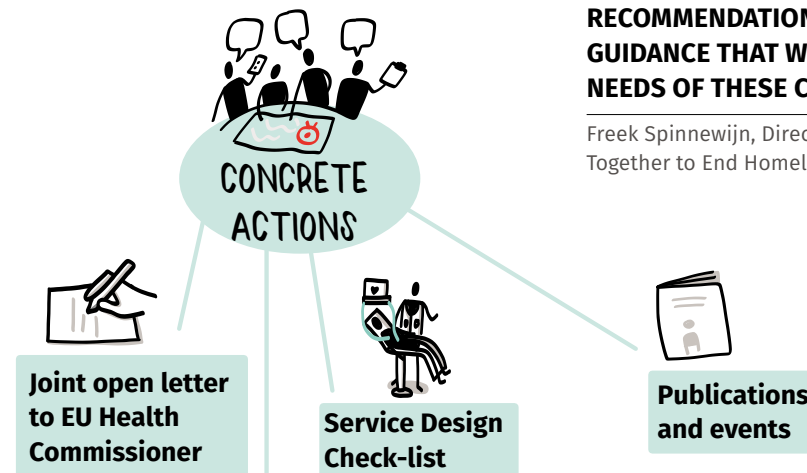
Even in high income countries, a large number of people are underserved by our health systems. This is particularly true for some of the most vulnerable and socially excluded groups such as LGBTBI, sex workers, migrants, homeless, people who inject drugs, and prisoners.

Underserved groups are often described as ‘hard to reach’, whereas, from their perspective, it is frequently the health services that are hard to reach. Highly stigmatised, they face a complex interplay of organisational and legal barriers in accessing healthcare.

In 2017, MSD kick-started an initiative with a group of NGOs representing these communities under the banner ‘Nobody Left Outside’. These organisations work together to identify shared challenges, discuss lessons learned through years of engagement, and seek integrated solutions to improve access to healthcare for the communities of people they represent.

THE AIM OF ‘NOBODY LEFT OUTSIDE’ IS TO ACT AS A UNIFIED VOICE AT THE EUROPEAN LEVEL TO IDENTIFY COMMON BARRIERS AND TO OFFER RECOMMENDATIONS FOR POLICIES AND GUIDANCE THAT WILL BEST MEET THE NEEDS OF THESE COMMUNITIES.

Freek Spinnewijn, Director FEANSTA, Working Together to End Homelessness in Europe



NOBODY LEFT OUTSIDE

For more information about Nobody Left Outside actions and founding organisations, please visit <https://nobodyleftoutside.eu/>



NOBODY LEFT OUTSIDE WAS SELECTED AS A THEMATIC NETWORK BY THE EU HEALTH POLICY PLATFORM FOR 2019

To learn more about MSD for Mothers, visit <https://www.msdformothers.com/>



HEALTH LITERACY

Health literacy empowers patients and citizens to play a more active role with regard to their health.

Health literacy is the ability to read, understand and act on health information. Over the years, MSD has been involved in a number of initiatives to promote better health through health literacy initiatives.

Nearly half of all Europeans have inadequate and problematic health literacy skills (The European Health Literacy Survey.) Limited health literacy in Europe is thus not just a problem of a minority of the population. It is a public health challenge.

HEALTH LITERACY IS A STRONGER PREDICTOR OF AN INDIVIDUAL'S HEALTH STATUS THAN AGE, INCOME, EMPLOYMENT STATUS, EDUCATION LEVEL, RACE OR ETHNIC GROUP.

Dr. Barry D. Weiss in "Help Patients Understand – Health Literacy Educational Toolkit", American Medical Association, 2007

HEALTH LITERACY SOURCES & DRIVERS

- SOCIAL DETERMINANTS
- NEWS MEDIA
- PATIENTS GROUPS
- PHARMA INDUSTRY
- EDUCATORS
- HEALTHCARE PROFESSIONALS
- FAMILY & CARE GIVERS

HEALTH LITERACY HEALTH OUTCOMES

- LOWER OVERALL COST
- EFFICIENT USE OF CARE SERVICES
- REDUCED REPEAT PROCEDURES
- OPTIMISED THERAPY
- REDUCED RISK BEHAVIOURS
- IMPROVED QUALITY OF LIFE
- MAKE THE HEALTHY CHOICE
- STAYING HEALTHY



ABOUT MSD

MSD is an innovative, global healthcare leader with over 125-year history of commitment to improving health and well-being for people and animals around the world. **Our core mission is to research and develop innovative medicines, vaccines, and animal health products.** We are pushing the boundaries of science with the hope and expectation that the medicines and vaccines we invent will lead to better health for society for generations to come.

We also demonstrate our commitment to increasing access to healthcare through far-reaching access programmes that bring our products to the people and animals who need them.¹

MSD operates in more than 140 countries to deliver innovative health solutions. Worldwide, MSD employs more than 69,000 people, of which 18,600 are based in Europe. **Our facilities are located in 26 of the 28 EU Member States.**

Our values guide everything we do, and they serve as the foundation of trust. We recognise that a variety of perspectives is crucial to encourage innovation. We therefore strive for **equal representation across our company, while promoting the best talent – as reflected by our 50/50 gender balance.**

FOCUS AREAS

MSD is focused on addressing many of the world's unmet medical needs. We are pioneering new approaches to prevent and fight cancer, challenging Alzheimer's disease, helping ease the impact of diabetes, preventing and treating infectious diseases, and helping more women have safe and healthy child-births. MSD also plays an indispensable role in developing vaccines for emerging global health crises, such as Ebola.

MSD. Inventing for Life. For more information, visit www.msd.com.

MSD IN NUMBERS IN EUROPE

- MORE THAN **18,600** EMPLOYEES IN EUROPE
- ABOUT **27%** OF OUR TOTAL WORK FORCE
- WITH A **50/50** GENDER BALANCE
- PRESENT IN **26** EU MEMBER STATES
- WITH **23** MANUFACTURING SITES

¹ See MSD Corporate Responsibility Report 2017/2018, available at <https://www.msdrresponsibility.com/access-to-health/research-development/>



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In case you have a question on one of the topics covered in this Policy Passport or any other issue related to pharmaceutical policy, please contact one of our colleagues below.

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“PHARMA” IN A NUTSHELL

The main objective of research-based pharmaceutical companies is to turn scientific insights into products and services that health professionals can use to treat patients. This takes decades of hard work and significant investments without any certainty of success.

At MSD, we aspire to improve access to health by discovering, developing and providing innovative products and services that save and improve lives.

PHARMACEUTICAL INNOVATION IS ONE OF THE GREATEST ACHIEVEMENTS OF OUR SOCIETIES

FOR PATIENTS



PATIENTS LIVE LONGER, HEALTHIER, MORE PRODUCTIVE LIVES

FOR SOCIETY



BETTER HEALTH IS A PILLAR OF OUR ADVANCED SOCIETIES AND IS CRITICAL FOR OUR ECONOMIC GROWTH



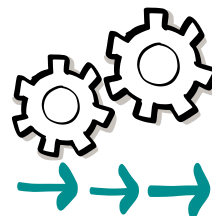
PHARMACEUTICAL INNOVATION

FOR HEALTHCARE



NEW TREATMENTS SUPPORT RESPONSIVE AND SUSTAINABLE HEALTHCARE SYSTEMS

FOR ECONOMIES



BIOPHARMACEUTICAL COMPANIES CREATE HIGH VALUE JOBS AND KEEP THE EU AS A GLOBAL CHAMPION