



FARMINDUSTRIA

NEXT GENERATION PHARMA

*A Future-proof
Pharmaceutical Industry*



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INTRODUCTION BY THE PRESIDENT

The pharmaceutical industry is already part of the future. It is today, in fact, that therapies are being developed to treat those who will need them in ten years' time. Moreover pharmaceutical companies operate on a global scale, recognising in advance innovation originating anywhere in the world.

Even more at this absolutely exciting historical phase, when the biopharmaceutical innovation is engaged in the development of over 7,000 products. An exponential acceleration that has no precedence in history, triggered by open innovation and by synergies unthinkable only a few years ago, like those with ICT companies that emphasise Big Data and encourage precision medicine. Very rapid transformations, with a strong thrust toward discontinuity, which must be anticipated to turn them into opportunities for companies and for the society.

Advancements in medicine, in fact, are not the target but the tool to improving people's lives. This is why the pharmaceutical industry is an asset for our country. An industry that invests and innovates: besides making even more effective therapies available, it creates economic, scientific and occupational value.

It is thanks to the joint commitment of institutions and companies that in the last few years significant steps forward have been made, in terms of both international prestige and credibility. Excellence in biotech medicines, advanced therapies, orphan drugs, plasma derivatives, vaccines and clinical studies constitute evidences that we can be a hub

not only of manufacturing – where we are leaders in Europe – but also of research.

Italy is acknowledged internationally as a reference point for innovative medicines and new technologies that allow better treatments and measurable results along the entire healthcare path. Now we need a more modern governance, which evaluates medicines on the basis of their clinical outcomes and of the many savings they bring about in other socio-healthcare areas. Because what matters for sustainability is the overall cost of healthcare, not that of individual treatments.

It is the direction suggested by the European Health Ministers for *"The next generation of health reforms"*. It is a challenge that Italy can doubtlessly overcome to the benefit of people's health, the sustainability of the National Health Service and the country's competitiveness.

Massimo Scaccabarozzi, President of Farmaindustria



01

A GREAT OPPORTUNITY

Chapter edited by Symbola - Foundation for Italian qualities

Convergence. In recent history the great technological discontinuities have originated from convergence phenomena: between knowledge disciplines, technologies, manufacturing systems and lifestyles. Today these processes experience an acceleration and scope (in terms of breadth of sectors and contexts involved) unthinkable until now. Digitalization, after a turbulent initial stage, now certainly facilitates and stimulates the transformation, hybridization and reconfiguration of productive chains. Production goes digital, products merge with services, technologies incorporate a human dimension, genomics embraces Big Data, digital platforms focus on people's health. In other words, bits meet atoms and reshuffle the cards. Facebook, owner of the world's most popular mass medium, does not create contents. Alibaba, the largest retailer, does not carry any inventory. Airbnb, the largest supplier of hotel facilities, has no real estate of its own. Uber, the world's largest taxi company, does not own any vehicles. Amazon digital store is opening "physical" bookshops. In other words, change is at hand and, if seized, it can be a great opportunity.

Who will drive the change. According to the dominant narrative, the big digital players colonise the sectors they approach. But facts tell us a different story. Apple was born as a computer manufacturer, then embraced convergence by selling music through iTunes and today it is practically the world's largest individual bond fund: convergence. Other companies, Lego above all, have also been able to

ride the digital innovation without losing their soul and without becoming a prey: Lego has merged its philosophy and digital technologies and has shifted the paradigm by offering, in addition to its products, also online services, from cartoons to videogames apps. If, therefore, "convergence" is the word of the day for the future ahead, the game for who will govern this convergence in the various sectors, and the pharmaceutical one first of all, is open: pharmaceutical companies in Italy have the skills and the energy to win, and they have already taken the challenge. There is a characteristic that makes the pharmaceutical industry different from other sectors: the importance of regulations. For this reason the success of transition will also depend on how institutions will be able to facilitate innovation without affecting what has been accomplished so far. Ensuring access to therapies and attractiveness for investments on innovation will both be crucial. To understand which are the trends and innovations the pharmaceutical industry will face in the next years, Fondazione Symbola has conducted a survey for Farindustria with the help of ten experts: a summary is given below.

A great discontinuity. There are many signs indicating that the pharmaceutical industry is also on the verge, if not already at the start, of a great discontinuity: in the last few years digital investments in healthcare have more than doubled, to over \$6.5 billion. Artificial intelligence has been the subject of academic discussions since the Fifties. It became known to the larger public on February 10th, 1996, when Kasparov

was defeated at chess by Deep Blue. However, only today artificial intelligence assists BlackRock in the management of one tenth of the funds in its portfolio, only today it assists physicians at the Institute of Medical Science of Tokyo University or those at the Memorial Sloan Kettering cancer centre in New York in their diagnoses: it appears that the era of A.I. (Artificial Intelligence) is here now. All the big players in the new technologies have started to deal with e-health.

A new context. If we place all of the above in a social and technological context in which – due also to the spread of wearable devices – the collection of data relating to our biometric and biomedical parameters and the disclosure of personal health information on the social media contribute to the daily global output of 2.5 exabyte of data (2.5×10^{18}); in a medical-scientific context making unthinkable progress in the knowledge of our genome, and sequencing it now at the same cost of a high-end smartphone (in 2003 the first complete mapping cost \$100 million); if we place all this within the framework of an information system where the computing power – that of a chip, under Moore's law, doubles every 18 months – allows us to make sense of this infinite amount of data; if we do all this, then we will be able to get an idea of the great acceleration that marks the changes we are witnessing.

Not unknown. As former U.S. Secretary of Defence Donald Rumsfeld once noted, “There are also unknown unknowns [things] we don't know we don't know. And [they] tend to be the most difficult ones”. Before we can deal with the less predictable

variables, the “unknown” ones – which will develop over a long period of time – let's start with the analysis of the “not unknown” variables, those innovations that are already on our radars: from the new role of patients empowered by digitalization, to the Big Data players and the web platforms, to industry 4.0.

The new players. In January 2001 iTunes was born, the first online shop for (legal) music downloads. By the end of the same year, iPod, the first digital music players, was placed on the market. In the same year a new big player, one that major companies and consumers would have to deal with, entered the music world: Apple. Nothing can be taken for granted – everything will depend on who will take the lead in the convergence – but the innovations that we are going to outline could produce similar effects in the pharmaceutical world, bringing in new actors and reconfiguring the value chain within the boundaries of one of the most regulated manufacturing industry.

The patient as protagonist and disintermediation.

Digitalization and the increased demand for connectivity and information is revolutionising the role of consumers. It is a change that increases their sense of *empowerment*: more and more, people want to be able to manage directly the processes and choices that affect them. It is a change that will have a deep impact on many healthcare-related services. Another ongoing change is that which starts a new age in the management of patients' data. Successful companies with great experience in gathering users' data are already active in this area, such as Google, Apple and

also Alibaba. Companies built around user experience and profile are the new players approaching the world of pharmaceuticals and healthcare.

Health within reach of a smartphone. We are used to book flights and hotels with our phones when we travel, to purchase goods or make bank transfers all by using our smartphones. Following the rules of disruptive innovations on the web – more efficient, simpler and cheaper services – it is not difficult to predict that, as for tourism and shopping, there could be service platforms that, with the assistance of a physician and on the basis of our clinical history (and perhaps our DNA), will remind us which medical examinations to do and when prescribed medicines must be taken, will suggest where to have our tests made, will notify and advise us on how to improve our lifestyles. On a different scale, something like this already exists: there is a multitude of apps – over 250,000 – dedicated to health.

The data age. An ever growing quantity of data is being generated these days but only a minimal part gets analysed, understood and integrated. Just think of the data generated by sensors and smartphones, medical devices, clinical files, web forums and social networks – nearly one patient out of three discusses health issues online – not to mention those relating to genomes (4 GB per capita).

The Real World Evidence. An example of innovation enabled by connectivity are contact lenses for diabetics developed by the cooperation (convergence) of some of the biggest pharmaceutical

companies with Google and DexCon. Such lenses measure the level of glucose in lacrimal fluid constantly and they are connected to a small sensor which calculates the levels of insulin and sends them to the cloud. A continuous monitoring that allows the patient to control insulin levels by an app, reducing the need for blood tests and providing physicians with information of unprecedented quality. It is a huge body of data that represents for medicine what is now referred to as Real World Evidence. Data that can rewrite some of the laws that regulate the Pharma world: the concept of outcome-based payments is already gaining ground, and Italy is at the forefront of this development.

Unknown. After the “not unknown” variables we come to the “unknown” ones: those that may already be present in research labs and of potentially huge impact, but that will be developed in the long term and with unforeseeable repercussions on the lives of people and on the pharmaceutical sector. We are talking about research on artificial intelligence and cognitive systems, we are talking about scientific discoveries in the field of gene editing and nanotechnologies, for which there is not yet a defined industrial perspective.

Artificial intelligence. Algorithms and digital systems that simulate cognitive abilities that are the prerogative of living beings take their names from these abilities: so we speak of artificial intelligence, or cognitive systems. Through training (machine learning), these algorithms learn by results: among the

most innovative ones are Generative Adversarial Networks (GANs), which work with two competing neural networks which progressively fine tune their own abilities. Basically all main players in digitalization are working on this: from Google with Deep Mind to Intel which in 2015 acquired the cognitive computing start-up Saffron, to IBM with Watson.

Watson and the others. Watson exploits an enormous computing power and an immense, constantly updated database, also with non structured texts: Watson “knows” over 700,000 scientific articles and 90,000 pathological cases, 25 million Medline abstracts, over 150 medicine books, 200 industry magazines, more than 4 million patents, data on over 10,000 pharmaceutical products and biological information relating to over 35,000 genes. No human being could do the same. Thanks to systems like Watson or those developed by *Insilico Medicine* or the London start-up *BenevolentAI*, a researcher in a pharmaceutical company could be helped when testing millions of molecules produced by basic research, and will be able to observe their properties and compatibility with the targets, identify candidates on the basis of potential therapeutic indications, predict their pharmacological dynamics, anticipate their toxicities and even make predictions on their chances of being admitted to clinical trials and of their final success. A physician could be helped, as it happens already in some centres, in reading test results, making diagnoses, and in choosing pharmacological therapies. The promise of these systems is particularly that of reducing times and costs of research, minimising failures.

Reading Big Data. According to Forbes, by 2020 – in 3 years from now – around 1.7 MB of new information for each human being will be produced every second. Who will interpret these data? Who will tell us what they mean and how to use them? Who will guide precision medicine in the choice of therapies that are less and less “one-fits-all” and growingly tailored on genetic profiles instead? The answer to these questions, once again, is the machine learning. And it is Big Data itself that is at the basis of the great opportunities that artificial intelligence promises to bring about, especially in medicine. Only by comparing an ever higher number of medical reports Watson is able to help a physician in making a diagnosis, only by “studying” huge quantities of data on the effects of medicines in real life it can help in the discovery of a new active ingredient. If artificial intelligence will live up to its promises, having access to data and relations with those who collect and manage them – will be a crucial asset for the pharmaceutical world: pharmaceutical companies will have to become data centric

The content or the container? Marketing teaches us that the container is everything, that the eyes and hearts of consumers perceive first the packaging and then the quality of what it contains. There is no doubt that the efficacy of a pill depends on its content, that is on its active ingredient: today the content becomes increasingly more important and the delivery of a medicine to the exact point where it has to act becomes the secret of tomorrow's medicines.

Smart pills and vectors. For years research has focused on the targeted function of medicines by designing smart pills that release the active ingredient only in a specific context or at a precise time; or that, when taken once a month, release a daily dosage of medicine every day. The potential of vectors has also been investigated in research laboratories: be they segments of carbon nanostructures, like fullerenes, or of liposomes to be targeted to specific types of tissues, it seems clear that when these “postmen” become perfected and trained, those who have created them will become a new ring in the chain. The efficacy of medicines – and perhaps even their cost – will depend on this.

CRISPR. On a more disruptive level, even though at an initial stage, there are the applications of CRISPR – Clustered Regularly Interspaced Short Palindromic Repeats – genetic sequences discovered by Francisco Mojica in 1993. The CRISPR-Cas9 gene editing technique is in fact the basis of a “cut and paste” kit of genetic sequences to operate with precision on a specific gene: to cut it to make it inactive (to “silence” it, as biologists say), or modify it according to need by changing even just a single letter in the sequence. Other techniques are used to edit genetic material but this one presents enormous advantages: as most classic disruptive innovations, it is simpler, more effective, faster and less expensive. In fact this technique is widely used today in laboratories across the world. The potential of the CRISPR-Cas9 is clearly enormous and it affects the entire field of medicine and a very wide spectrum of diseases. For example,

scientists at the Irvine University of California have demonstrated the possibility of modifying the germinal line of the *Anopheles stephensi* mosquito with the CRISPR-Cas9 system: modifications of this type in the future could prevent the transmission of malaria thus eradicating it. The future of this technique is doubtlessly man, with all the ethical questions it raises.

Solution companies. In this scenario of strong acceleration, as we have already said, the future of the pharmaceutical industry and its role in the convergence is yet to be written. There are two main recommendations to navigate the convergence safely. The first one comes to us from Bill Gates: “There are only three things that matter for the success of an organisation: *people, people, people*”. The second is to think of themselves not as enterprises based on products but as “solution companies”. For example: diabetes – which affects 387 million people and accounts for up to 10% of the healthcare expenditure – is a medical condition requiring integrated solutions for patients. Not just a medicine but services that support them throughout their lives and improve their quality of life, with the non-negligible benefit of reducing social and healthcare costs. The pharmaceutical industry may not be able to lead in each one of these innovations, but it can become the driving force that rides the age of convergence by widening its perspectives – as it is in part already doing – to new actors and new fields: by making hybridization a new industrial strategy, with a mindset which is gradually less oriented towards just products and increasingly human-centred.

02

**RESEARCH,
ITALY AS AN
INTERNATIONAL HUB**

Research is Life. Medicines and vaccines contribute to our health on a daily basis. A result that is clearly visible in the story of those who, in spite of illness, can continue to plan their own future, thanks to the commitment of companies, which fund more than 90% of research.

Living longer and more actively. In the last 50 years life expectancy in Italy has increased by 1 month every 4, a phenomenon to which pharmaceutical innovation has contributed and continues to do it significantly, over 70% since 2000. An improvement of all Advanced Economies, stronger in Italy, that is also affecting developing countries progressively.

The renaissance of research. Pharmaceutical R&D is experiencing a Renaissance age: it is proven by the historic record of medicines in the pipeline at global level, with over 14,000 products under development, more than 7,000 out of which at the clinical phase. Research focusing mainly on oncology, neurology, infectious, metabolic and muscular-skeletal diseases, and trying to find answers for many other pathologies.

From new molecules to incremental innovation.

Treatments can thus become reality, giving hope of a longer and better life for millions of people. First of all thanks to the great “leaps forward” in therapies, the breakthrough innovation, but also thanks to the improvement of those already available: in fact, 63% of pharmaceutical products listed in the World Health Organisation Essential Drug List come from “incremental” innovation.

R&D highlights

Today 2 people out of 3 who are diagnosed with cancer survive for at least 5 years. 30 years ago the statistics were 1 in 3 (83% of this improvement is due to new medicines)

Today hepatitis C is curable. HIV has become a chronic disease: a 20-year old who is diagnosed with the disease has a life expectancy of 70 years

Today, compared to 10 years ago, mortality for chronic diseases has decreased: by 33% for cardiovascular diseases, 35% for respiratory diseases and 31% for metabolic diseases

Vaccines prevent infectious diseases and some types of cancer, they ensure control of target diseases, in some cases until eradication of the disease (i.e. smallpox)

Today, over-65s who declare to be in good health in Italy account for 29% of the total, they were 18% 10 years ago (an improvement of 1.8 million people)

In 2016 pharma companies in Italy invested €1.5 billion in R&D (17% of value added); researchers are 6,200, 52% of them are women

Italian excellence in: biotech medicines, orphan drugs, plasma-derivatives, vaccines, clinical trials and advanced therapies (3 out of 6 in Europe were developed in Italy)

Every year pharma companies in Italy invest €700 million in clinical trials. For every euro invested in oncology trials, the national health service saves €2.2.

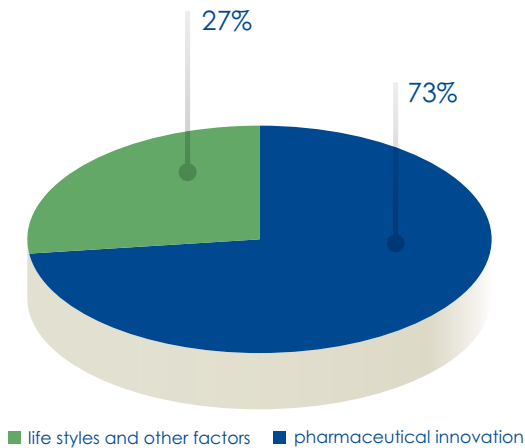
Increasing number of answers to health needs. Many medicines today are available to treat diseases incurable in the past, and others that block their progression or prevent complications. Thanks to a higher degree of precision than in the past, as demonstrated by the number of orphan drugs, with more than 200 medicines designated by EMA for the treatment of rare diseases. And also as shown by the increase in personalised therapies: more than 20% of the products authorised in recent years and 42% of those under development, a percentage that reaches 73% for oncological treatments.

Biotech medicines: the future is already here. The new treatment perspectives are offered in particular by

biotech products, which represent 40% of the pipeline, a percentage that is destined to increase. Biotechnologies are already the present of pharmaceutical research and will be even more important in the future, for example to treat rare diseases, for which they are often the only possible treatment.

Greater attention to women's health. The analysis of the relationships between gender and the efficacy of treatments is essential to the well-being of men and women. This is why growing attention is paid to the health of women, with 850 medicines in development worldwide for diseases ranging from diabetes to cancer and from muscular-skeletal to autoimmune diseases.

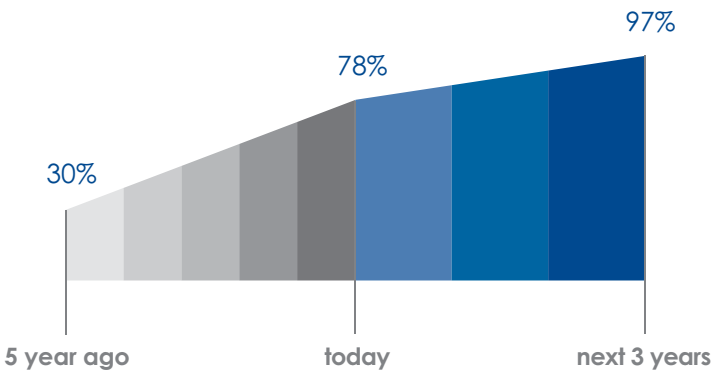
FACTORS CONTRIBUTING TO THE INCREASE OF LIFE EXPECTANCY IN ADVANCED ECONOMIES SINCE 2000



Source: Efpia 2017

SHARE OF PHARMA COMPANIES IN ITALY ENGAGED IN R&D IN BIOTECH, ADVANCED THERAPIES OR RARE DISEASES

(data weighted for R&D investments)



Source: Farindustria – Bain & Company

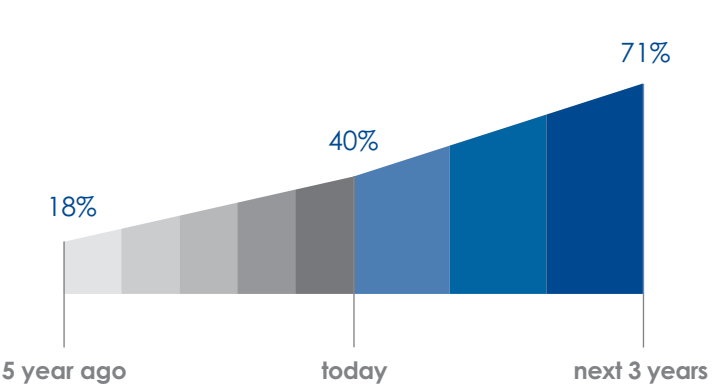
From mapping to editing of genome: the revolution of Life Sciences. Technological progress allows us to foretell the achievement of the genome sequencing at sustainable costs in the near future. This will allow the combination of genetic and clinical data with data on lifestyles and health conditions to improve prevention and diagnosis.

A future marked by precision medicine. At the same time research has demonstrated that the efficacy of medicines is not the same for everyone but that it varies from person to person. Thanks to the analysis of the human genome it is now possible to draft more targeted and more effective therapies, reducing the chances of side effects. For this reason efforts in

research today are focussing on the identification of outcome-predictive biomarkers for a specific pharmacological treatment.

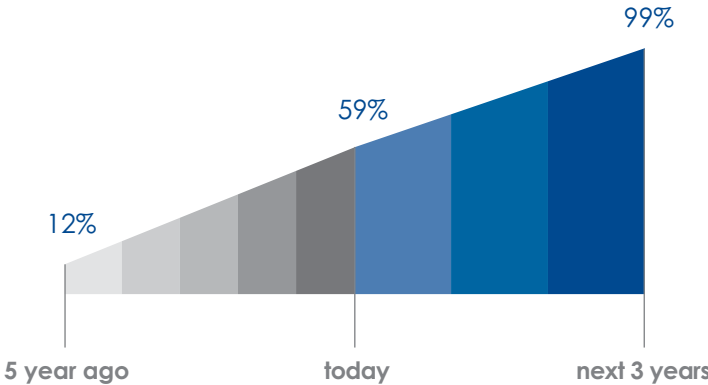
Big Data changes the way research works. To memorise the information of the genome of individuals a great deal of data will be produced: this is why biopharmaceutical research is one of the fields of greater application for *Big Data* and why medicine and ICT are interconnected. There are even more partnerships among the major pharmaceutical companies and the giants of new technologies ("healthcare disruptors"), to build cognitive systems supporting the choices of doctors and researchers.

SHARE OF PHARMA COMPANIES IN ITALY IN WHICH DIGITAL INNOVATION HAS AN IMPORTANT ROLE IN R&D ACTIVITY
(data weighted for R&D investments)



Source: Farindustria – Bain & Company

SHARE OF PHARMA COMPANIES IN ITALY ENGAGED IN REAL WORLD EVIDENCE STUDIES
(data weighted for R&D investments)



Source: Farindustria – Bain & Company

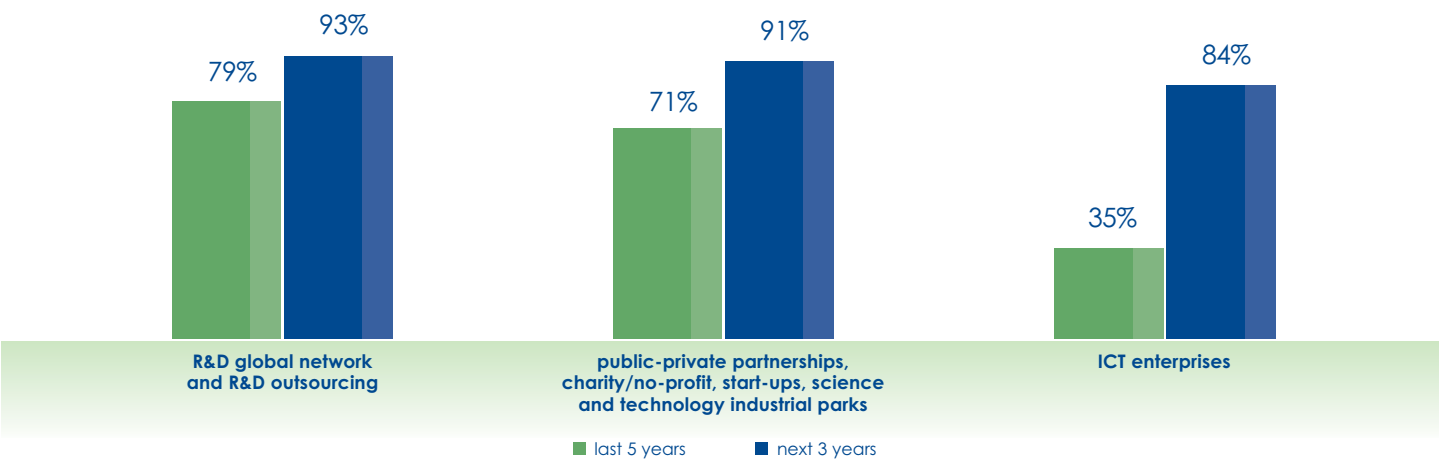
Research is growing multidisciplinary. New medicines are developed through an ever deeper knowledge of how the biological processes, that need to be cured and corrected, work. In such a scenario the winners are - and will be even more often - small and focused research teams, with a multidisciplinary approach going beyond the traditional boundaries of medicine, through cooperation between doctors, mathematicians and bioinformatic specialists. To increase the knowledge of the links between DNA, lifestyles, environments and diseases.

The paradigm shift: Open Innovation. The need to access to the best available know-how at every stage of research determines a new and deep

transformation of worldwide supply and demand of innovation. 80% of today's pharmaceutical innovation comes from partnerships between large companies, SMEs, public and private centres of excellence, in particular in the biotech sector.

The engine of innovation. This global "market of ideas", offers the Italian system great opportunities, more than in the past. The links between pharmaceutical companies, biotech PMIs, start-ups, universities, clinical centres of excellence, non-profit organisations – both in basic and applied research – represent the engine of innovation in Life Sciences. It is here that investment is needed to benefit from the great wealth of know-how already in the country.

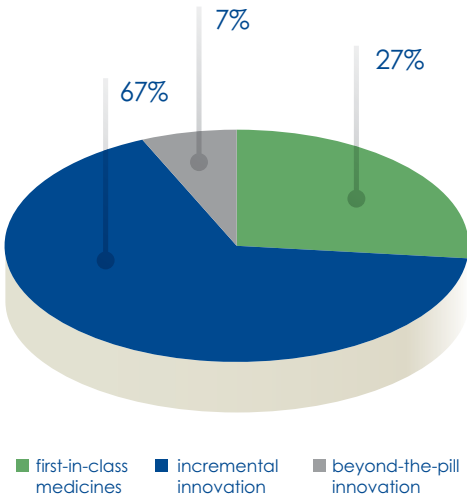
SHARE OF PHARMA COMPANIES IN ITALY CONDUCTING R&D IN PARTNERSHIP, BY TYPE OF PARTNERSHIP
(data weighted for R&D investments)



Source: Farindustria – Bain & Company

A continuous commitment to research. In 2016 pharmaceutical companies in Italy invested €1.5 billion in research, with an increase of 20% over the last three years. The pharmaceutical industry holds a leadership position in Italy: it invests 17% of added value in R&D, 12 times the national average, leading the country towards the target of 3% of GDP in R&D fixed by Europe 2020. Company data reveal that the role of first-in-class medicines (those that start a new class of products) has greatly increased in the last few years, as has that of beyond-the-pill innovation, related to the integration between medicine and digital devices, with the purpose of improving the patient's health outcome (adherence to therapies, for instance).

5 YEARS AGO: COMPOSITION OF PHARMA COMPANIES R&D INVESTMENTS IN ITALY

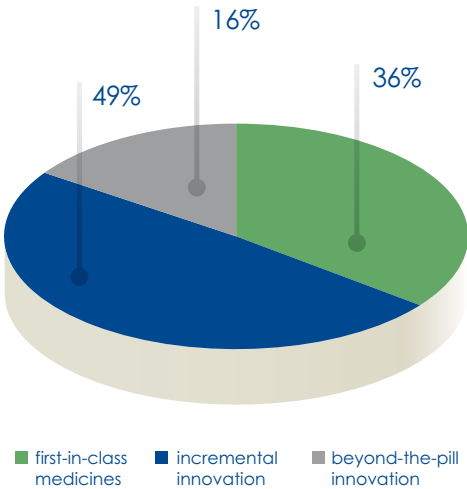


Source: Farindustria – Bain & Company

Research in Italy is a worldwide protagonist. In addition to the high quality of academic research, the R&D of pharmaceutical industry in Italy is specialised in biotechnologies (with over 300 products under development), vaccines, plasma derivatives, orphan drugs, and gender medicine. It leads advanced therapies: in fact, 3 out of the 6 authorised in Europe originated from R&D in Italy.

Companies' investment strategies. In the last 10 years externally-conducted R&D has increased by 95%, mostly thanks to clinical studies. Partnerships and the innovation network have grown. Increasingly with ICT companies.

TODAY: COMPOSITION OF PHARMA COMPANIES R&D INVESTMENTS IN ITALY



Source: Farindustria – Bain & Company

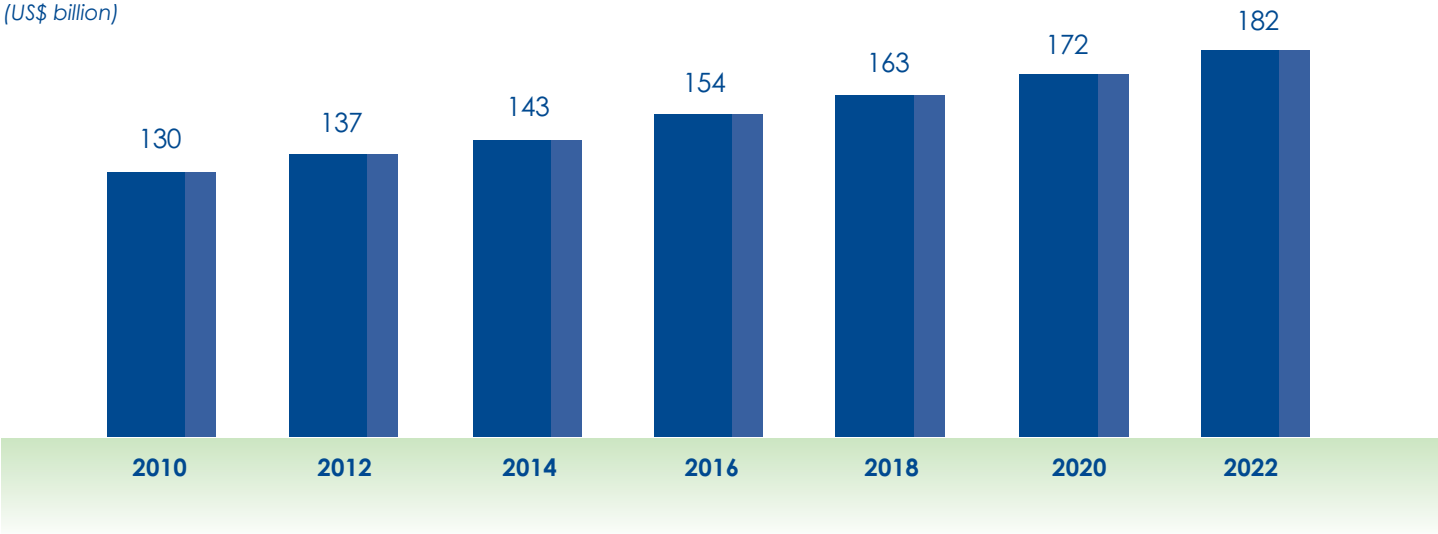
What are clinical trials? They are studies on the safety and efficacy of medicines, carried out on volunteers only after having collected sufficient information on the characteristics and safety of the product, and after the authorisation by an Ethics Committee that evaluates the competence of researchers, the suitability of the trial and ethical aspects, including the informed consent, respect for privacy and insurance requirements.

Significant resources for the country. Investments in research at global level will soon reach \$180 billion and now companies are investing already around \$100 billion in clinical trials: an opportunity for Italy with its solid scientific know-how and excellences in its universities and in the structures of its national health

service. The pharmaceutical industry invests €700 million a year in clinical trials in the country, the highest contribution to the national research system. Such contribution can grow further with more effective authorisation procedures.

Benefits for patients and for the National Health Service. Clinical trials make innovative therapies available to patients; they offer the possibility of professional growth to physicians and researchers, they ensure significant resources and fewer costs for the National Health Service, because companies underwrite all the related expenses, such as hospitalisation, medicines and diagnostic tests. According to estimation, for every euro invested in oncology clinical trials, the system saves €2.2.

WORLDWIDE PHARMACEUTICAL R&D INVESTMENTS
(US\$ billion)



Source: Evaluate Pharma

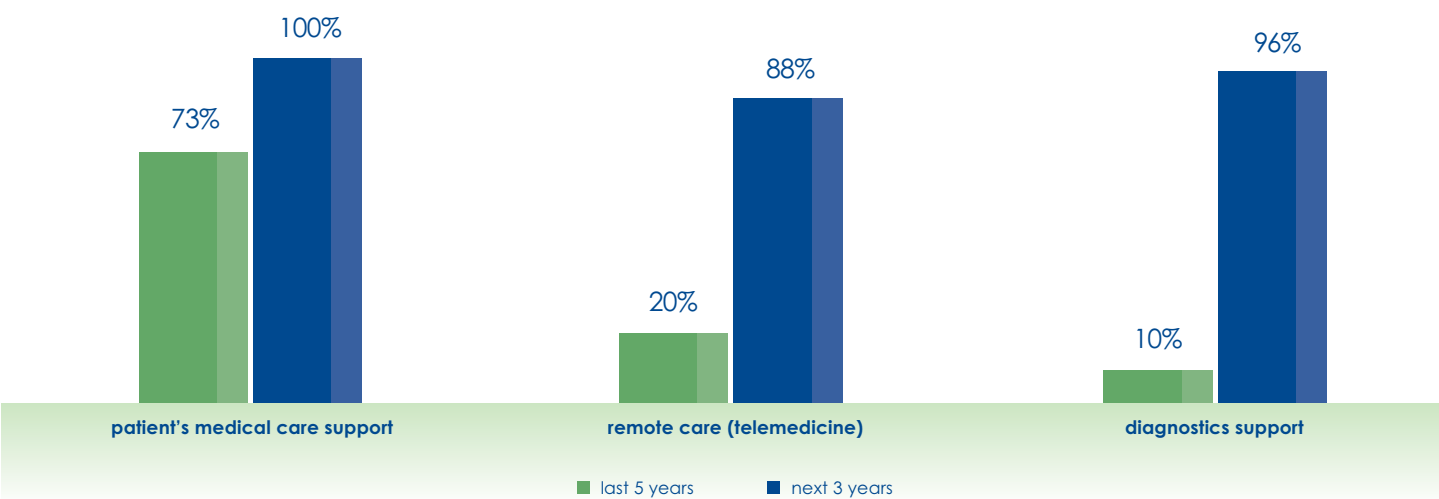
Greater patient engagement thanks to ICT. Digital technologies available today are reshaping the relationship between patient and physician in the process of medical treatment and assistance. The citizen becomes thus “empowered”, i.e. able to interact in a more aware and responsible manner with the doctor and the National Health Service in general. A valuable contribution to his own health and the scientific community.

A changing concept of health. All these transformations go along with the change in the concept of health: from condition of absence of pathologies to that of a state of physical, psychic and social wellbeing. A holistic approach that puts the person at the centre, stressing the importance of

lifestyles, prevention and healthcare education. The schemes of stakeholders is also modified: for example by fully recognising the role women play as caregivers, in the management of the health of the whole family.

New medicines and new instruments supporting treatments. In such a new landscape companies increasingly offer e-health products and services in support of patients’ care and treatment, from remote monitoring of health conditions, to the remote provision of medical assistance (telemedicine), diagnostic systems that collect and elaborate data from digital supports (digital diagnostics) and make data available in real time to healthcare professionals (electronic clinical files).

SHARE OF PHARMACEUTICAL COMPANIES IN ITALY OFFERING E-HEALTH PRODUCTS AND SERVICES FOR PATIENT'S CARE SUPPORT
(data weighted for R&D and gross fixed investments)



Source: Farindustria – Bain & Company

03

**THE PHARMACEUTICAL
INDUSTRY,
CHAMPION OF
“MADE IN ITALY”**

An engine of the growth of the country.

Especially in the last few years, pharmaceutical companies in Italy have been a fundamental engine for the economy. From 2010 to 2016 the pharmaceutical industry led the manufacturing sector in terms of growth of exports, added value and competitiveness. 2017 has also been marked by a positive start in terms of production, employment and exports.

Among the top European players. The sector has recorded brilliant results also in Europe, thanks to investments and sales abroad. These results place Italy among the great European players, with a production worth 26% of the total of big European countries and exceeding its market share (19%). That is why today our country is an international hub for the production of medicines and vaccines, which are exported all over the world. An asset of the industry in Italy and Europe.

A mix of national and foreign-owned companies that strenghtens our industry. The strength of the pharmaceutical industry in Italy comes from a unique composition in Europe, 60% of foreign-owned and 40% of Italian-owned companies. These companies – regardless of the nationality of their capital – are among the best of “Made in Italy”, because they invest, create employment, generate industrial and scientific culture and are geared towards international markets.

Production highlights

The value of production is €30 billion, of which 71% for export (€21 billion). Considering the upstream sector, the overall value amounts to €44 billion

Italy ranks 2nd among big European countries in terms of value of production, after Germany (€31 billion), and before France (€21 billion), UK (€20 billion) and Spain (€16 billion)

+52%: growth of pharmaceutical exports in Italy from 2010 to 2016, higher than the European average (+32%) and the overall Italian manufacturing average (+24%)

64,000 direct employees and 130,000 including upstream sectors. Employment growth at 1% per annum in the last two years (12,000 new jobs, half of which under30)

€2.7 billion in investments in 2016, €1.5 billion in research and €1.2 in production. This value has been growing by €450 million in the last three years (+20%)

Pharma ranks first among all industry sectors in Italy in terms of growth of industrial production (19%) and export from 2010 to the first quarter of 2017

Pharma is the top manufacturing sector in Italy in terms of investments and exports by foreign-owned companies, exporting over 90% of their production

70%: share of export on total turnover of Italian-owned companies, thanks to a strategy of internationalisation that enhances the value of activities in Italy

Productivity increases, surpassing that of big European countries.

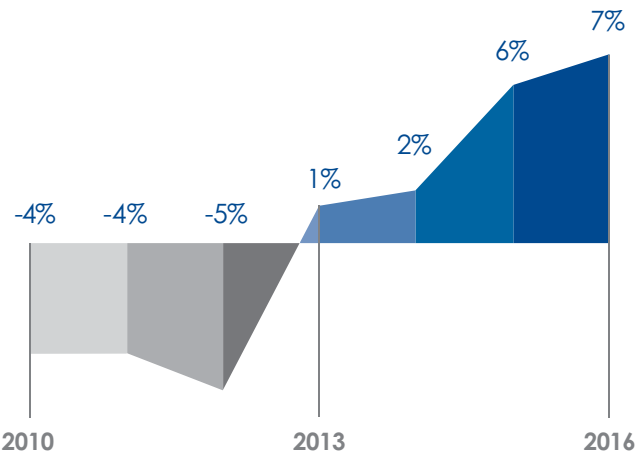
The quality of human resources, the high industrial know-how and the investments of pharmaceutical companies boost productivity and allow the industry to overtake the average of the big European countries. Pharmaceutical manufacturing registered a relevant growth, too, entirely due to the increase of exports.

The value of the pharmaceutical sector multiplies with upstream activities. Manufacturers of raw materials, machinery, processing and packaging technologies, components and services for the industry, constitute a sector of excellence at a global level, with €14 billion

worth of production, 66,000 employees and over €800 million in investments – which contribute to multiply the value generated by pharmaceutical companies.

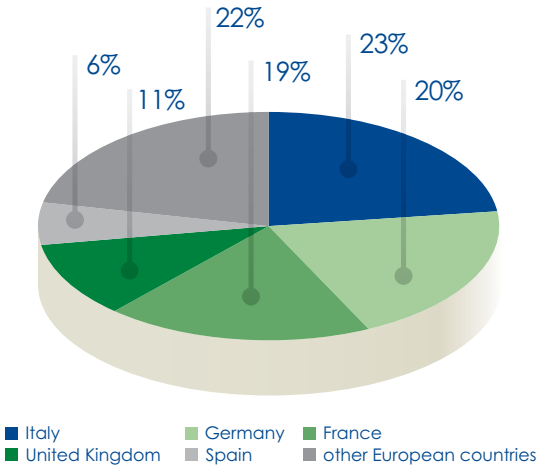
An industry that benefits the country. Strongly concentrated in five regions – Lombardy, Lazio, Tuscany, Emilia Romagna and Veneto – but also present in Piedmont, Abruzzi, Marche, Campania, Sicily and Apulia, the pharmaceutical industry represents a value for the territory, through the activation of a wide network of stakeholders: from the upstream companies to institutions, to school and universities, public, private and non-profit health organisations

PHARMA COMPANIES: LABOUR PRODUCTIVITY GAP BETWEEN ITALY AND OTHER BIG EUROPEAN COUNTRIES
(value added/employee)



Source: Farindustria elaboration, Eurostat data

ITALY RANKS FIRST IN EUROPE FOR VALUE OF PRODUCTION OF PHARMACEUTICAL CONTRACT DEVELOPMENT AND MANUFACTURING ORGANIZATION



Source: Farindustria – Prometeia

Investments, innovation, growth. 29% of the increase in production in the last 5 years comes from the launch of new products, 16% from the attraction to Italy of activities previously carried out in other countries. A factor that translates into growth in investments: +20% in three years, on products and processes of high innovative content and with greater added value. During the same period, nearly all companies have renewed their plants and 94% of them is ready for further investments in the near future.

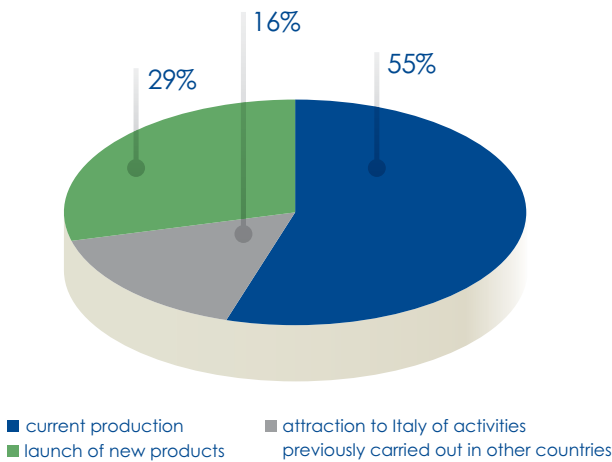
The pharmaceutical industry in the digital and Industry 4.0 era. Pharmaceutical companies are

already at the forefront of digitalization of productive and organisational processes. With software for integrated plant management, intelligent logistics, additive manufacturing (e.g., 3D printing) or virtual prototyping technologies.

Leading the environmental challenge.

Environmental awareness has always been very strong in the pharmaceutical industry and today this sector is among the *greenest*: first in growth of investments in clean technology since 2010 and in reduction of energy consumption in the last 10 years (-63% compared to an average of -25%).

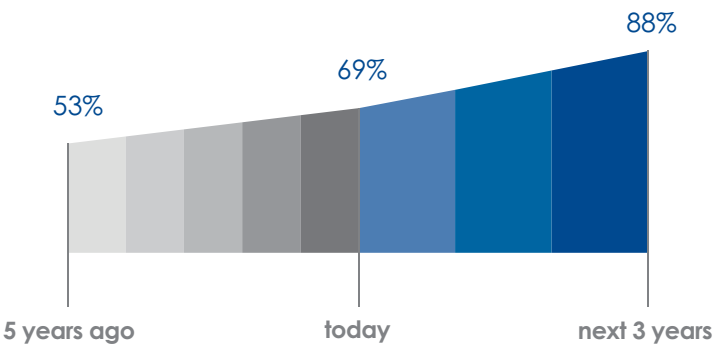
COMPOSITION OF GROWTH IN PHARMACEUTICAL PRODUCTION IN ITALY IN THE LAST 5 YEARS



Source: Farindustria – Bain & Company

SHARE OF PHARMA COMPANIES IN ITALY IN WHICH DIGITAL INNOVATION IS WIDESPREAD IN PRODUCTION PROCESS

(data weighted for gross fixed investments)



Source: Farindustria – Bain & Company

Human resources, the main competitiveness factor.

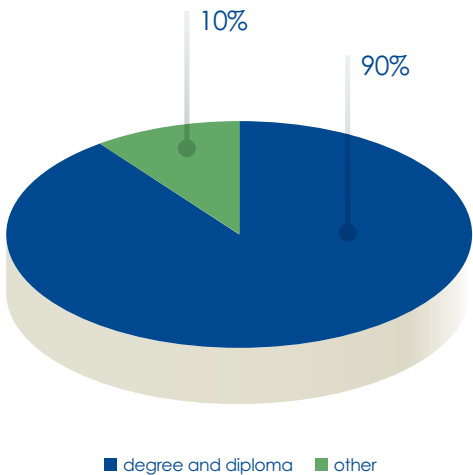
The business of pharmaceutical companies requires excellence at all stages: quality, training and skills of human resources are essential. Companies themselves consider these ingredients as the main reason to invest in Italy. Factors which, together with investments, determine a productivity that doubles the manufacturing average and the top position in the Istat ranking of competitiveness.

90% of employees have a degree or a high school diploma. In the last few years the pharmaceutical industry has increased its percentage of highly skilled employees, as shown also by the latest Istat competitiveness report. Furthermore, the Pharma

sector registered an increase in employment, in particular in production and research positions. In fact, since 2014 pharmaceutical companies have hired 6,000 people per year, 50% of whom under 30 years of age.

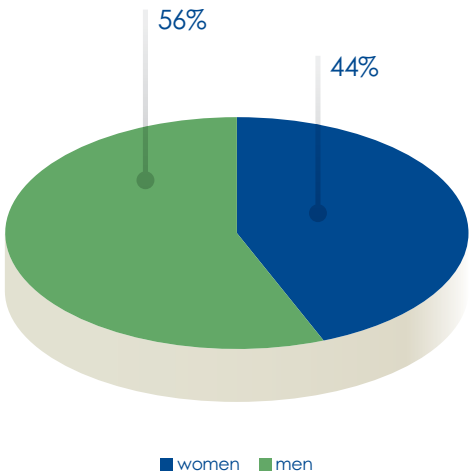
A success due also to women. In the pharmaceutical industry, 4 employees out of 10 are women, often holding positions of great responsibility. This is one reason why 77% of pharma companies offer welfare programs – compared to an industry average of 44% – to ensure balance between career, family and private life: training and educational services for children, nurseries, company canteens, wellness and prevention.

EMPLOYMENT IN PHARMACEUTICAL INDUSTRY IN ITALY BY EDUCATION LEVEL



Source: Farindustria

EMPLOYMENT IN PHARMACEUTICAL INDUSTRY IN ITALY BY SEX



Source: Farindustria

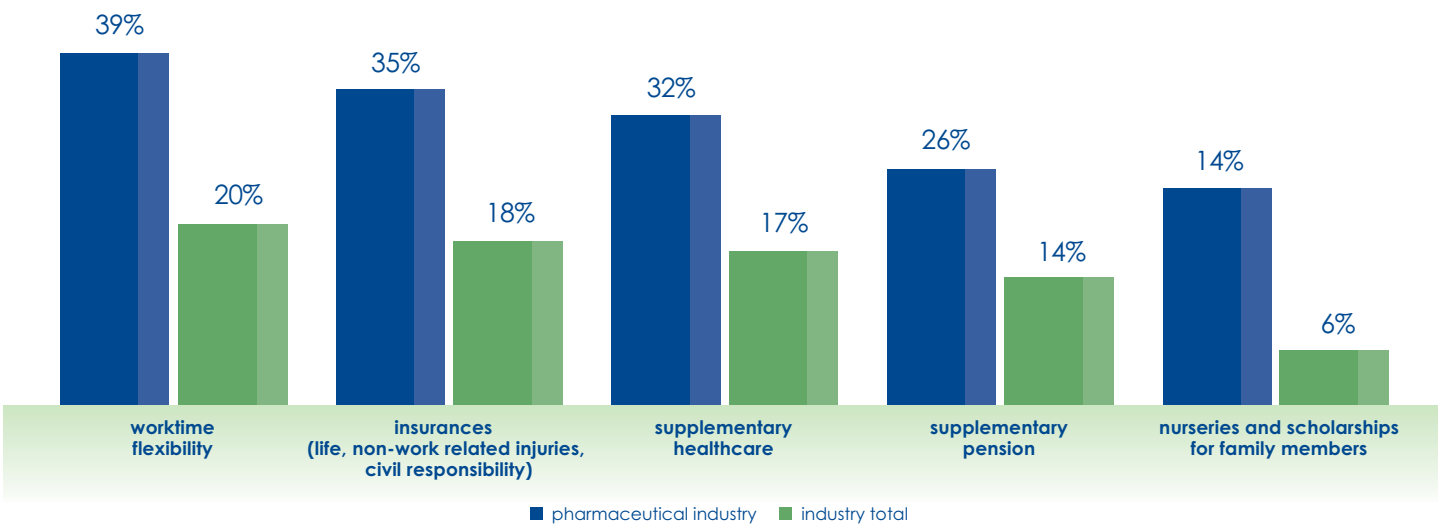
Industrial relations as a tool of growth. Innovative, participative and cooperative industrial relations foster the competitiveness of our companies, with flexible contracts and the concrete implementation of social responsibility. Collective bargaining allowed the creation of a modern and efficient welfare system, with three important tools: Fonchim (supplementary pension fund), Faschim (supplementary healthcare fund) and Welfarma (for the retraining and redeployment in the labour market).

School-work Programme. Introducing young people to the labour market is a national goal. Farindustria was the first trade association to join the pilot project

of the Italian Ministry of Education “Alternanza in Filiera” in cooperation with high school, technical and professional institutes and students of the Bologna-Parma and Latina-Pomezia pharmaceutical clusters.

The Farindustria training school for member companies. Since 2014, Farindustria has been offering the opportunity to new employees of its member companies to get a full picture of the sector, with the aim of having more knowledgeable and motivated professionals. Courses are delivered by Farindustria and company experts, university teachers, representatives of Aifa, Istituto Superiore di Sanità and the Confindustria System.

SHARE OF PHARMA COMPANIES IN ITALY PROVIDING WELFARE SERVICES (IN ADDITION TO THOSE PROVIDED THROUGH COLLECTIVE AGREEMENT)



Source: Farindustria

04

**ASSESSMENT
OF OUTCOMES,
A TOOL OF
SUSTAINABILITY**

Italy, world health leader. The National Health Service is one of the most important assets of the country. Many respected international sources (WHO and OECD to name but a few) rank Italy among the top countries for life expectancy in good health and quality of the health service. Medicines and vaccines play an essential role in achieving this result.

Comparison with Europe. Such excellent results have been obtained with a lower public spending than the average of big EU countries: 6.7% of GDP vs. 7.7%. A good signal for sustainability, but also a reminder that the funding of the National Health Service must be adequate to face the growing demand for health and to allow greater innovation.

The most controlled expenditure item.

Pharmaceutical spending is the most closely monitored item of public spending: completely tracked, with standard costs and binding spending caps - and companies reimburse the National Health Service for expenditure overruns – and medicine prices negotiated at national level and they are lower than the European average (-15%).

Lowest public per capita spending in Europe. In Italy, public expenditure for pharmaceuticals borne by the State is 29% lower than the European average: €288 per person compared to €405. Our country is in line with other European countries in terms of diffusion of equivalent (i.e. off-patent and generic) medicines and it ranks first in value and volume of sales for biosimilars, with the highest market share among the main European countries.

Expenditure highlights

Per capita public pharmaceutical spending in Italy is lower than in big European countries and 29% lower than the European average: €288 compared to €405

In the last ten years the pharma expenditure/GDP ratio has been stable at 1%, compared to 1.2% of big European countries; pharma production/GDP ratio in Italy is 1.8%

Appropriate therapies reduce hospitalisations with substantial savings. A day in hospital costs €1,000, nearly equivalent to 4 years of per capita pharmaceutical expenditure

€1 spent on vaccination generates benefits equal to €44: €16 by avoiding costs of the disease and the rest by increasing resources generated by healthy people

Oncology medicines represent 4% of the overall socio-healthcare costs and they can reduce the remaining 96%. The overall per capita exp. has decreased by 11% since 2010

Annual healthcare expenditure in Italy to treat hepatitis C patients is over €1 billion, which could be saved through medicines that could cure them, at the lowest cost in Europe

Off-patent medicines represent 90% of sales in pharmacies, in line with other big European countries (QuintilesIMS data)

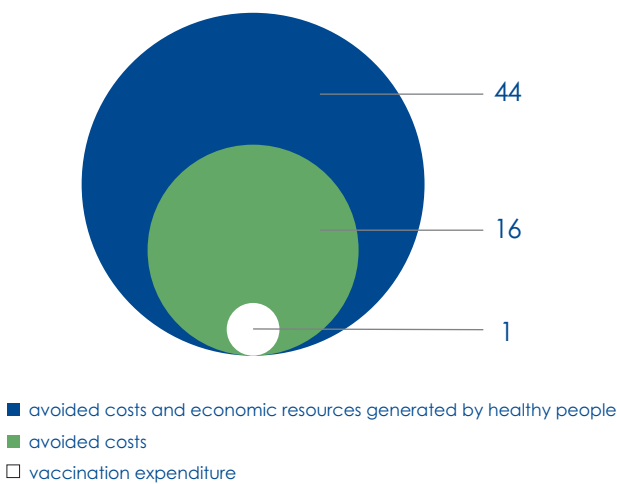
Italy ranks first in Europe for biosimilars sales, both in terms of value and number of units; Italy's market share is higher than the European average (26% vs 13%, QuintilesIMS data)

Savings from the appropriate use of medicines and vaccines. Medicines and vaccines reduce costs for the citizen and the National Health Service: for example, by rendering more expensive unnecessary services, by preventing diseases or by slowing their progression, as in those typical of ageing, thereby postponing the need for care. Moreover, better treated patients can often handle the disease while continuing to work and maintain an active role in society. A benefit to the entire country, in the framework of increasing patient involvement and of citizen empowerment to improve prevention, early diagnoses and adherence to therapy.

Measuring outcomes improves care and optimises expenditure. Sustainability cannot be pursued by cuts

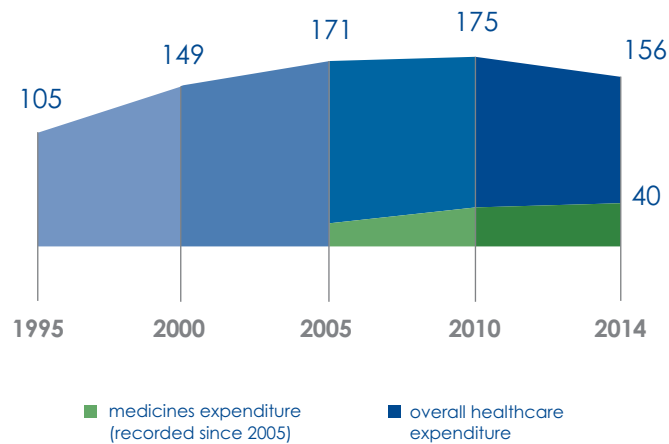
in spending, which in Italy is already much lower than the European average. The international debate stresses the need to measure the overall outcomes of treatments (outcome-based approach), rather than the cost of individual services. With assessment models based on the collaboration of all stakeholders and with an active role of pharma companies. On these models, Italy can be competitive at international level, also thanks to the work on registries done by Aifa in these years. A paradigm shift in this direction can lead to the effective modernisation of the system. That needs to be translated into government spending choices: to the benefit of healthcare and the sustainability of the National Health Service.

COST/BENEFIT RATIO OF VACCINATION



Source: Health Affairs 2016

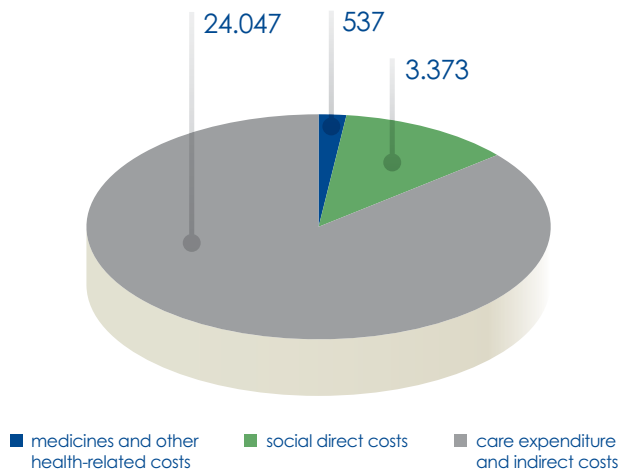
ONCOLOGY: PER CAPITA MEDICINES EXPENDITURE AND OVERALL HEALTHCARE SPENDING IN ITALY (€)



Source: IHE – Comparator Report 2017

New governance. Innovation poses new challenges for the National Health Service, requiring a more modern governance. The steps forward taken in recent years must soon be consolidated by an overall re-engineering of the system and by improving prevention and appropriateness of cures. Basic principles should be: sufficient funding for health demand; the confirmation of *ad hoc* resources for innovative medicines; moving beyond the concept of pharmaceutical spending caps (starting with spending for direct purchase); the protection of intellectual property and of investments; the uniformity of health policies throughout the territory, guided by scientific criteria; the recognition of innovation and an improved access to treatments.

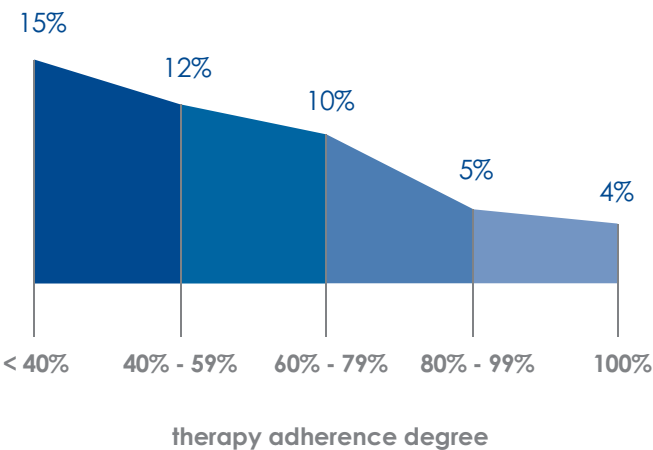
PER CAPITA EXPENDITURE FOR SENILE DEMENTIA IN ITALY
(€ per year)



Source: The Economist-Intelligence Unit 2017

Improving access to new medicinal products. In recent years, Italy has been more focused on innovation than it used to be in the past, with dedicated funding for innovative medicines and with the shortening of access times following EMA authorisation. However, access times still remain long (about 12 months) also because, in most cases, they must include the time for regional authorisation. These regional and local bureaucratic constraints create differences between citizens and limitations to the access to new medicines, as demonstrated by the per-capita consumption, which is significantly lower in Italy than in the rest of the big European countries.

HOSPITALIZATION RATE FOR DIABETIC PATIENTS



Source: PhRMA

05

FARMINDUSTRIA

Farindustria is the Association of pharmaceutical companies in Italy. It counts approximately 200 companies, representing over 90% of the sector in Italy. It is one of the main associations of Confindustria and in the leading group within the European Federation (EFPIA). It is also a member of IFPMA, the International Federation of Pharmaceutical Manufacturers and Associations.

The mission. It represents the voice of the companies operating in the country, it promotes competitiveness and scientific development and communicates their value to institutions, the public and stakeholders in order to promote a governance better facilitating investments and access to the new medicines. With Europe becoming more and more the center of economic decisions, Farindustria - that has its headquarter in Rome - has opened its own office in Brussels.

Communicating the value of the pharmaceutical sector in Italy. Since 2012 Farindustria has organized the roadshow “Innovazione e Produzione di Valore” to communicate the importance and the role of pharmaceutical companies in Italy. The roadshow has visited Tuscany, Emilia Romagna, Lombardy, Lazio, Apulia, Abruzzi, Marche and Campania, and it will move on to other regions with a strong pharmaceutical presence. There are several initiatives to promote the specific characteristics of the biopharmaceutical industry: biotechnology, vaccines, plasma derivatives and Contract and Development Manufacturing Organisation. To widen the tools to support this communication, since 2017 the Association has also

been present on social networks, with a Facebook page and a Twitter account coming soon.

The Association of 360° innovation. Research and innovation are the core business of pharma companies. Public initiatives and documents to the Institutions characterise Farindustria's work. The focus is also on cutting-edge topics such as Industry 4.0 and new health technologies, personalised medicine, open innovation and their regulatory and organisational implications.

Research meets health needs. Farindustria interacts with institutions and patient associations on topics of broad social relevance such as research, access to innovation, gender medicine and rare diseases. A closeness to people that also manifests itself with support for many initiatives aimed at fostering awareness of and respect for the needs of patients.

Teamwork with companies. Through 30 working groups, Farindustria provides services to its member companies on legislative, legal, regulatory, scientific and industrial relations aspects. It operates within the framework of one of the strictest Codes of Conduct in Europe, regulating relations between companies and between them and the world of science and healthcare. In 2016, the Association adopted the Disclosure Code, the Transparency Code of EFPIA, which requires companies to make data on the collaboration with doctors and their organisations public and accessible. The Code was firmly wanted by companies that, thanks to this instrument, can now be even more transparent, in a sector that is already very well regulated.

NOTES

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