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Paediatric Clinical Trials Extended Patent Protection – Driver of Innovation?

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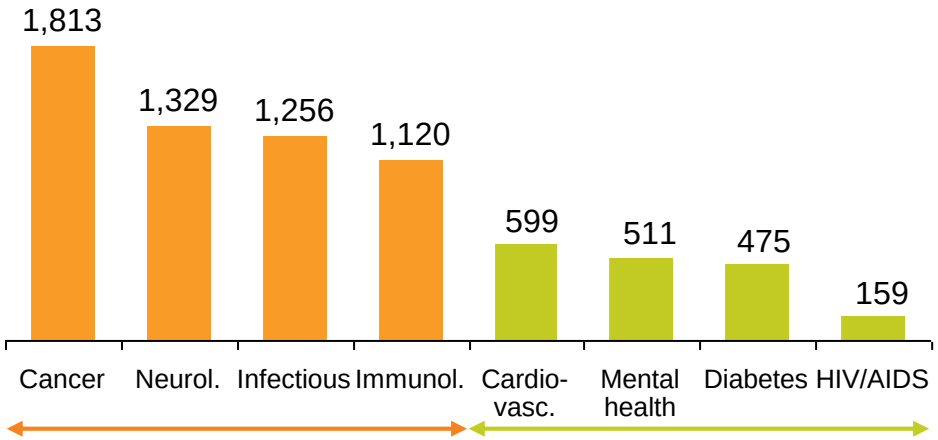
The evolution of science opens an exciting and challenging area of medical innovation, potentially addressing many unmet needs

Medicines in development worldwide[1-2]

* All therapeutic areas covered by today's pipeline were identified as unmet needs of society by the WHO in 2013[3]



Areas of high unmet need

* High disease burden
* Limited treatment options
* Breakthrough technologies

Key disease areas

* Large patient populations
* Long-term treatment
* Lifestyle & adherence focus

Overview of promising new technologies & complex diseases[4-7]

Gene therapy

* The first approved human gene therapy trial was in 1989[4]
* The first gene therapy was approved in the EU 23 years later[4]

Stem cell therapy

* The first human stem cells were isolated in 1998[5]
* The first stem cell-based therapy, restoring the eyesight of patients with severe cornea damage, was granted 17 years later[6]

Neurol. diseases

* For every medicine making it to market, ~30 failed to yield a new medicine to treat AD, in part due to disease complexity[7]
* Currently, 59 products are in development for AD & other dementias[7]

More than 7,000 medicines are currently in development, with the potential to bring hope to patients and foster sustainable health outcomes[2]

AD=Alzhemer's disease; WHO=World Health Organisation; source: 1. Health Advances analysis; 2. Adis R&D Insight Database (accessed 2015); 3. WHO. 'Priority Medicines for Europe and the World 2013 Update' (2014) 4. Hanna et al. J Market Access Policy (2016); 5. Thomson et al. Science (1998); 6. EMA, Holoclar (accessed 2017); 7. PhRMA. 'Researching Alzheimer's Medicines: Setbacks and Stepping Stone's (2015)

Pharmaceutical R&D is an increasingly resource-intensive and long-term process, with no guarantee of success

Growing trial complexity (2003-2011)[1]

25% increase in median clinical trial duration

48% increase in average number of eligibility criteria per trial (i.e. the allowed patient characteristics)

57% increase in the median number of procedures per trial (e.g. X-rays, blood tests, etc.)

211% increase in median number of case report form pages per protocol (a clinical trial form) from 55 to 171

Success rates from phase 1 to launch dropped by 29%, from 16.4% in 1996-1999 to 11.6% in 2012-2014[2]

Source: 1. Getz et al. 'Variability in protocol design complexity by phase and therapeutic area' (2011); 2. Smietana et al. 'Trends in clinical success rates'. Nature Reviews (2016)

The EU has refined the IP incentives and rewards system to encourage research into areas of unmet need

Overview of European IP incentives[1]

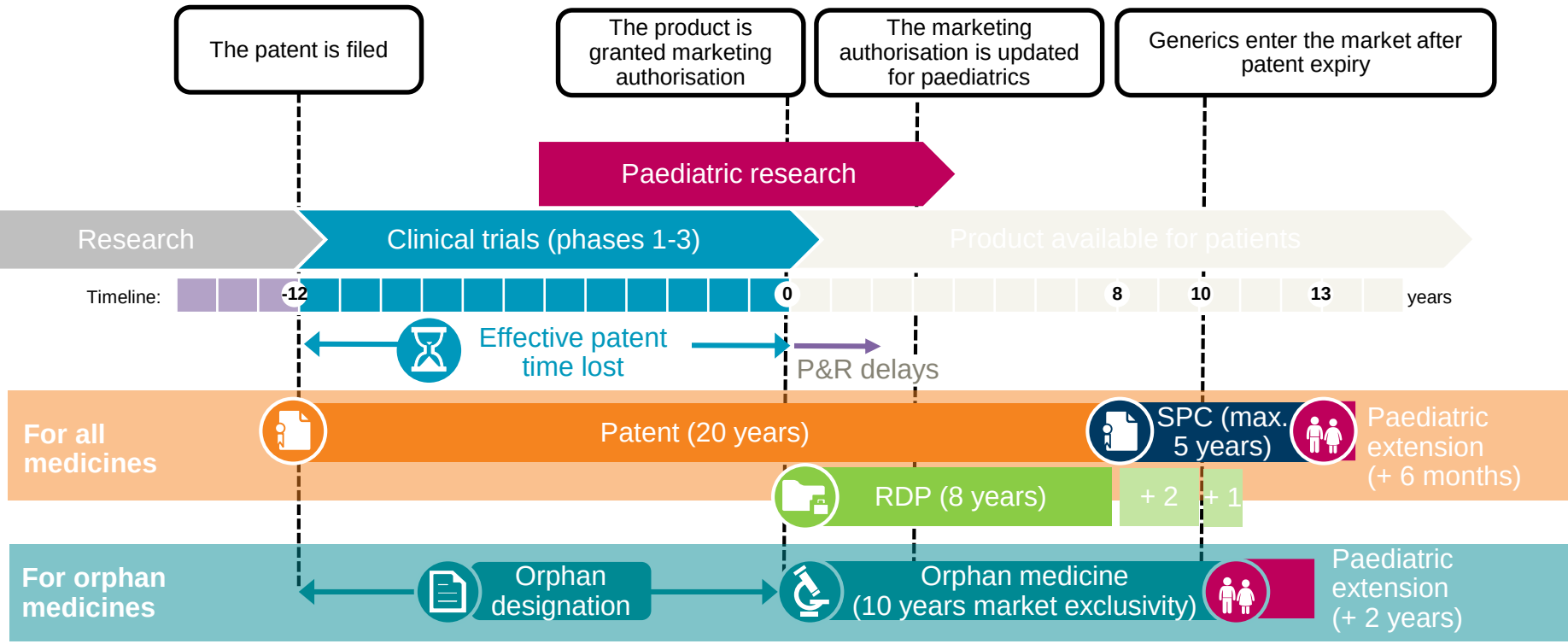
Patent (1474*)	Encourage companies to invest in R&D by protecting any invention from copies for a limited period of time during which the patent holder can ensure absence from unfair competition by manufacturers that did not have to undergo risky, expensive & complex R&D processes; in exchange for exclusivity, the investor makes the invention public so that more research can follow
Supplementary Protection Certificate (1992)	Extend exclusivity for a pharmaceutical product that is protected by a patent to compensate for part of the time lost during the lengthy development period before a medicine can be made available on the market and ensure sustainable funding for such research
Regulatory Data Protection	Protect product developers' investment to generate the pre-clinical and clinical data required to obtain a marketing authorisation from unfair commercial use
Orphan Designation (2000)	Incentivise companies to research and develop medicines for rare diseases by providing specific development support and protecting them once marketing authorisation is obtained from market competition with similar medicines for the same rare ('orphan') indications
Paediatric Extension (2007)	Reward companies for undertaking the significant additional testing needed to ensure the safety and efficacy of the medicine for children, as required under Paediatric Regulation

"[SPC] aims to guarantee laboratories working to develop new medicinal products a level of protection equal to that enjoyed by R&D in other sectors."[2]

*Italy
EU=European Union; IP=intellectual property; Source: 1. Manufacturer statement (2017); 2. European Commission. Proposal for a Council Regulation concerning the creation of a supplementary protection certification for medicinal products (1990)

IP provisions work side-by-side to enable pharmaceutical companies to continue innovating despite obstacles

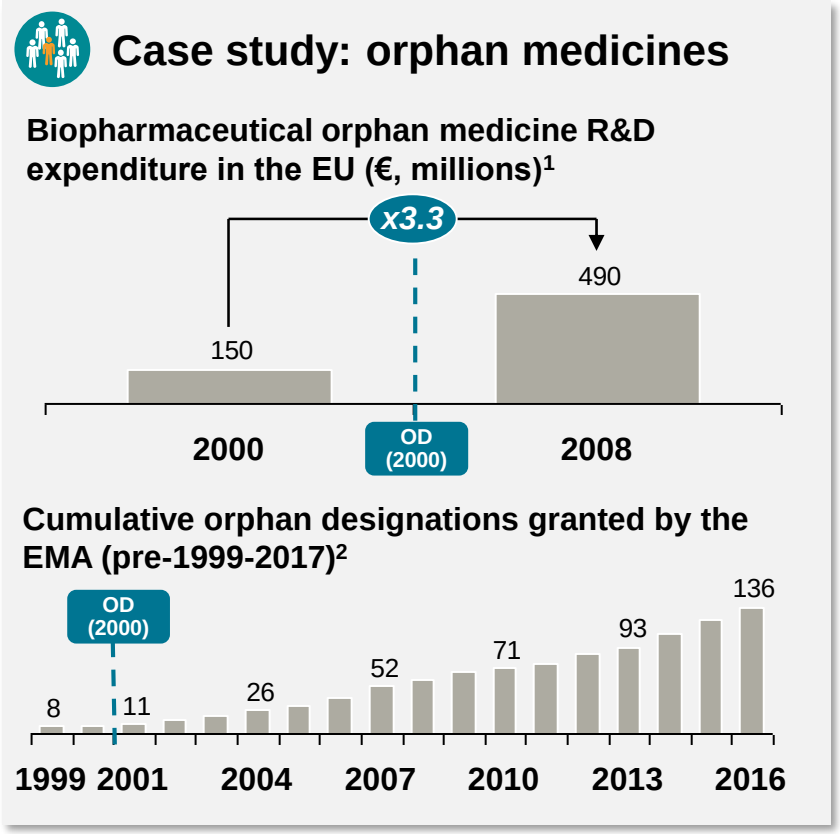
Application of IP incentives[1]



IP systems have been designed to foster and ensure the competitiveness of European countries for innovation

EU=European Union; IP=intellectual property; RDP=regulatory data protection; SPC=supplementary protection certificate
Source: 1. EFPIA, About IP incentives (2017)

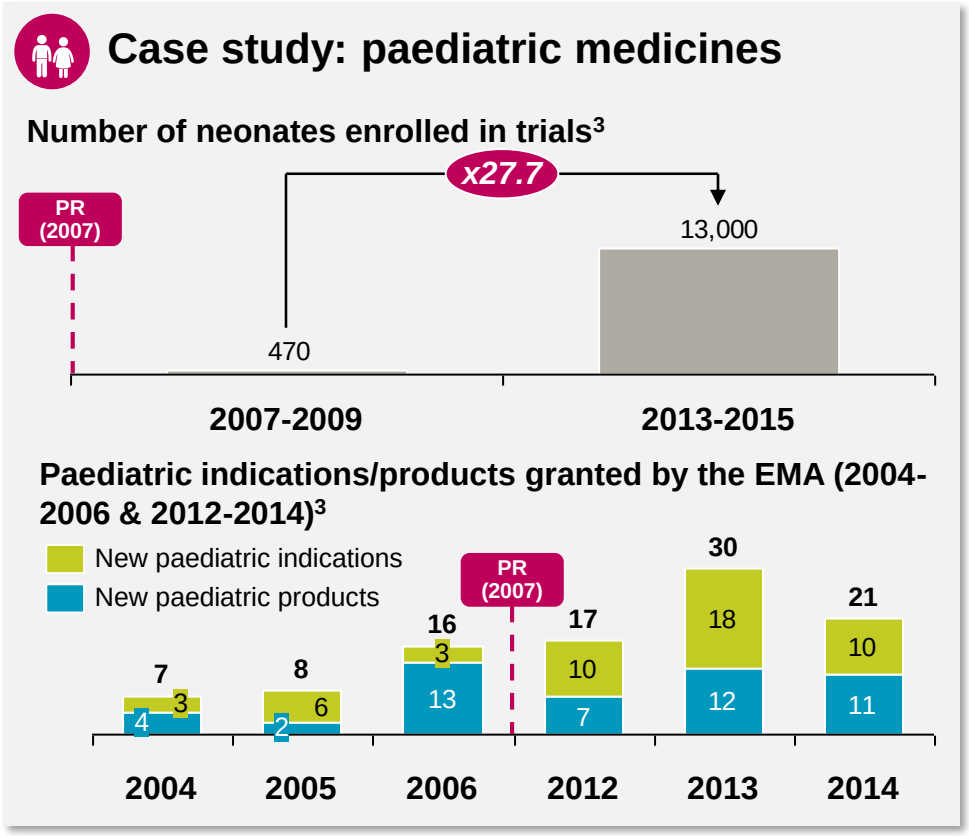
Orphan incentives have been key to foster innovative treatments for patients previously without options



Since the creation of relevant IP provisions, 220 new orphan-related SMEs were created (from 32 initially), and 68 paediatric-related SMEs (from 21 initially)[4]

OD=orphan designation; PR=paediatric regulation; SME=small- and medium-sized enterprise
Source: 1. Office of Health Economics (2010); 2. Charles River Associates. 'An evaluation of the broader economic and societal impact on orphan medicine regulation' (2017); 3. EMA. '10 year report to the EC'; 4. Charles River Associates. Analysis of EMA SME Register (2017)

Paediatric incentives have been key to foster innovative treatments for patients previously without options



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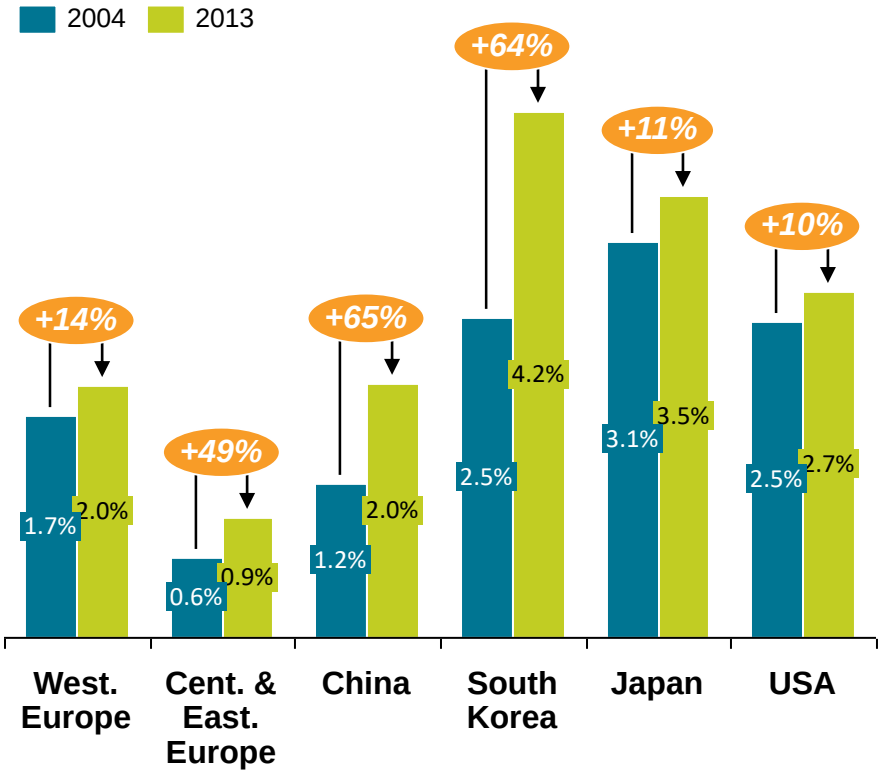
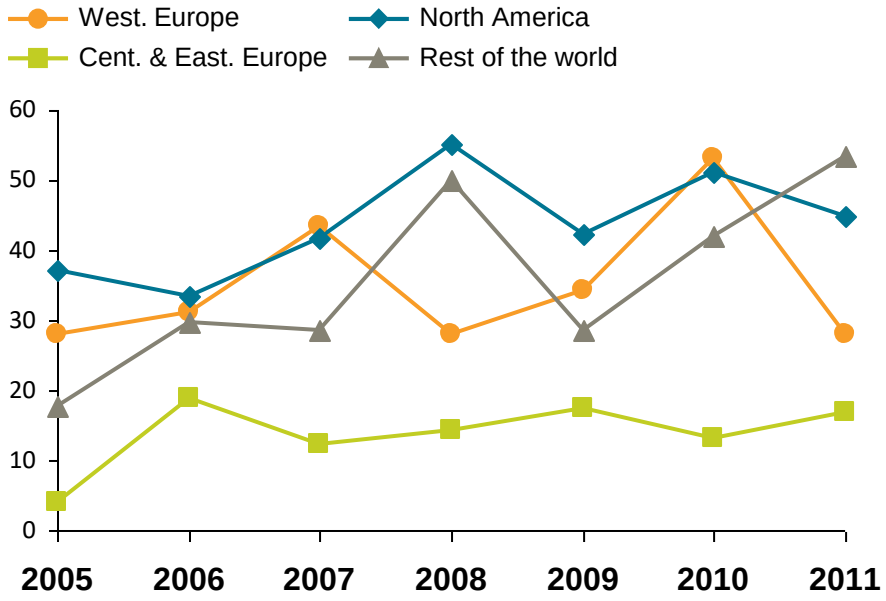
The competition for R&D infrastructure and skills is increasingly global, requiring countries to be attractive for investment

R&D* intensity as share of GDP (2004-2013)[1]



Investigator sites for clinical trials (thousands, 2005-2011)[2]



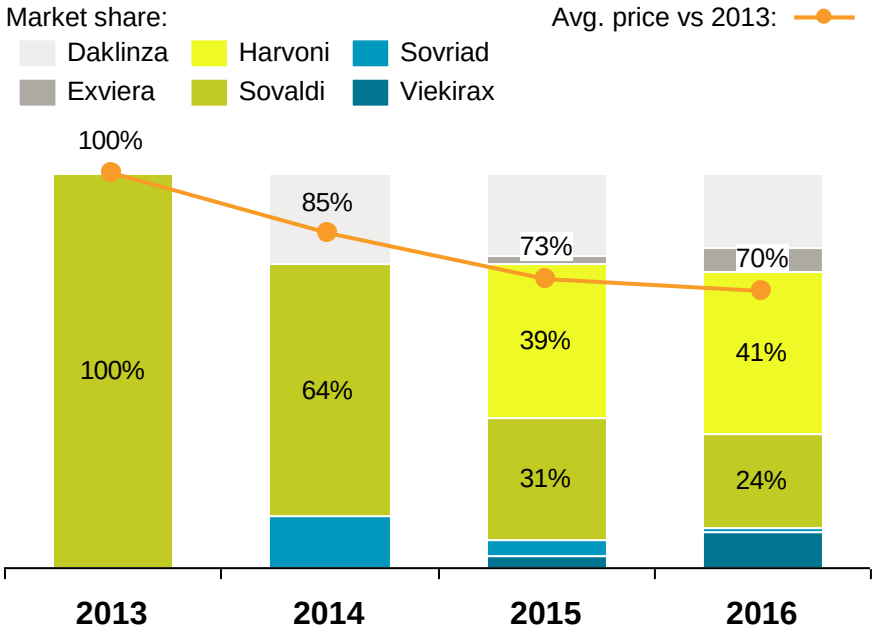
* Though Europe has indeed maintained its share of clinical trials, this is largely down to positive developments in Eastern Europe

From 2014-2015, there was a 6% increase in capital raised by European companies, compared to 35% increase in capital raised by US companies[3]

*Including all sectors, not just pharmaceutical; GDP=gross domestic product; R&D=research and development; Source: 1. OECD. Eurostat statistics; 2. EMA. Clinical trials submitted in marketing-authorisation applications to EMA (2013); 3. EY; Biotechnology report (2016).

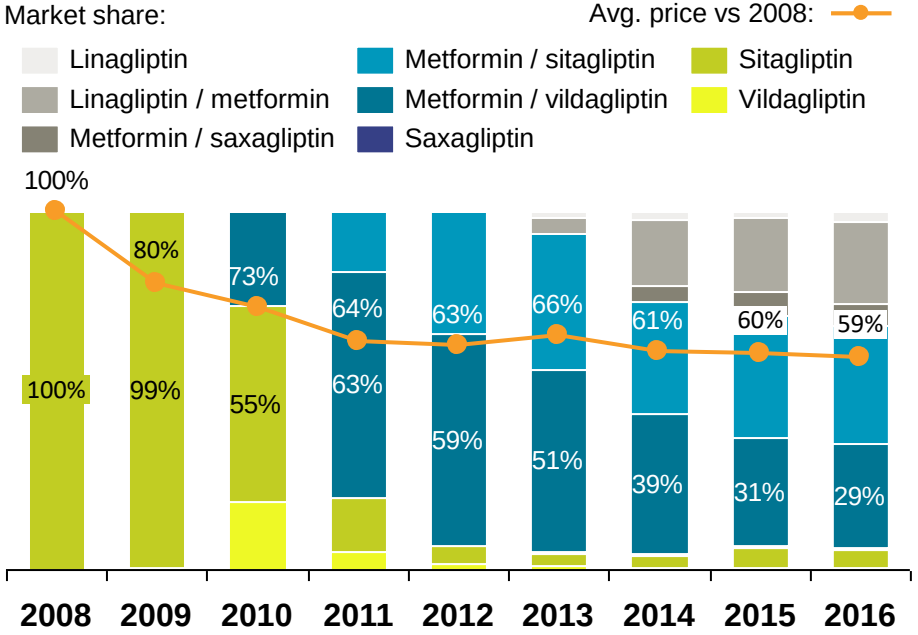
IP protection enables the innovation necessary to foster competitive conditions, in turn driving down medicines prices

Product volume market share & price for hepatitis C treatment in France*,1



* Over four years, the entry of five new competitors led to a 30% decrease in the average price of treatment

Product volume market share & price for anti-diabetics (DPP-4's) in Bulgaria*,1



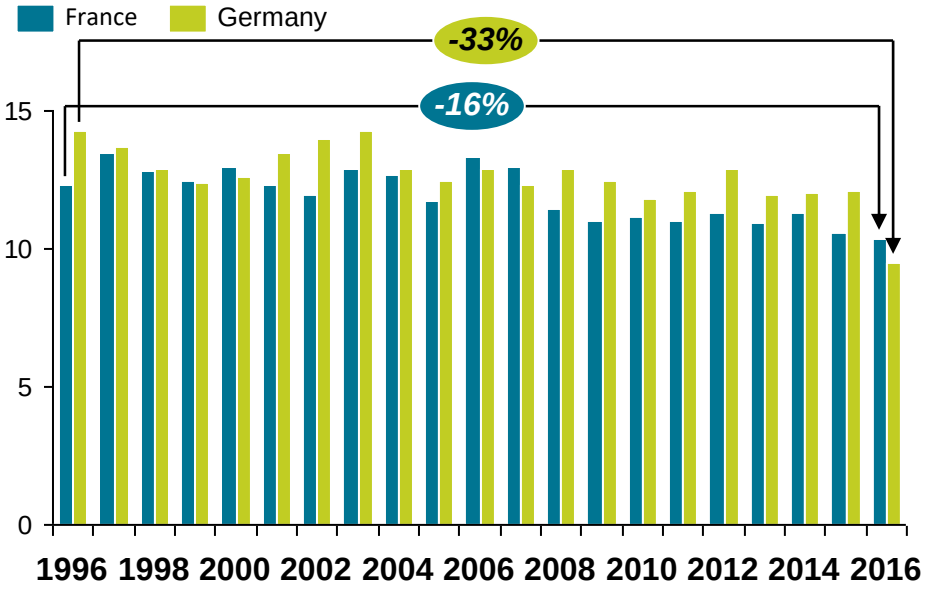
* Over eight years, the entry of seven new competitors led to a 41% decrease in the average price of treatment

IP and pricing are not linked: IP does not create a economic monopoly

*Ex-manufacturer prices; exclude rebates, discounts & other agreements
IP=intellectual property; NOAC=novel oral anticoagulant; CF=cystic fibrosis; CL=chronic lymphocytic leukaemia, PAH=pulmonary arterial hypertension
Source: 1. IMS. 'Theories of harm & key elements of response' (2017)

The time to generic entry varies mainly depending on commercial potential for generic manufacturers, P&R process & competition

Average time from launch to patent expiry, per NASs launch year cohort (years,1996-2016)[1]



* Exclusivity periods can vary by several years depending on the product and/or country, but are decreasing alongside an increasingly robust IP system

Key drivers of competition for generic medicines[2]

Size of market at originator loss of exclusivity

Price and volume competition
(i.e. generic relative to the brand at time)

Supply side factors
(e.g. P&R regulation, manufacturing difficulty)

Number of generic entrants

Demand side factors
(e.g. generic substitution)

From 2010-2014, loss of exclusivity in the EU saved EUR 70-110 million each year, offsetting the price of new medicines in 13 countries[3]

P&R=pricing and reimbursement
Source: 1. Data from QuintilesIMS MIDAS, analysis by EFPIA (2017); 2. Bianchi et al., 'Dynamics in the generic market: evidence from the UK', Office of Health Economics (2014); 3. IHI. The Role of Generic Medicines in Sustaining Healthcare Systems: A European Perspective (2016)

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Thank you for your attention