



Pharmaceutical Innovation in Europe

New pharmaceutical breakthroughs approaching –
is the system set up to fund them all?



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Executive Summary

The advent of new potential blockbusters in Europe is anticipated to position the pharmaceutical industry on a sustained growth pattern through 2022 (2015-2022 CAGR at 3.2%). While oncology is set to take the lion's share in terms of growth, innovations have been emerging across several therapy areas. Among the top 10 bestselling products in 2022 the crown is expected to move from Humira to Xarelto while five therapies will be addressing unmet needs in cancer. As the pharmaceutical pipeline continues to meet the demand for improved outcomes, question marks on the sustainability of the system as we know it continue to rise.

Methodology

The figures presented within this report are based on EvaluatePharma's European Drug Forecasts, the first European dataset based on government and company reported data and enabling a thorough horizon scanning of the European landscape by providing product level forecasts for 300 in-line and 500+ pipeline assets.

Sales projections to 2022 are based on consensus forecast information at Worldwide, Rest of World and European level and further modelled with Evaluate's proprietary inputs – trending of historical sales, analogue-based uptake and erosion curves, time to market benchmarks.

The following countries are included within the definition of Europe: France, Germany, UK, Italy, Spain, Sweden, Denmark, Finland, Norway, Poland, The Netherlands, Belgium, Greece, Switzerland, Austria, Portugal, Romania, Czech Republic, Hungary, Ireland, Slovakia, Bulgaria, Croatia, Serbia, Slovenia, Lithuania, Latvia, Estonia, Cyprus, Iceland, Malta.



2015-2022 European pharmaceutical industry on a sustained growth pattern

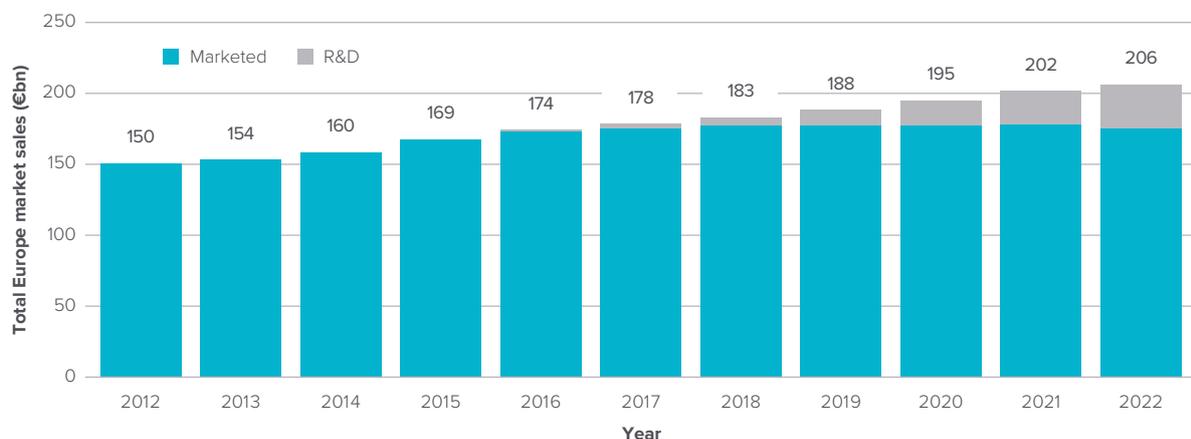
While the European macroeconomic outlook is quite gloomy, the pharmaceutical industry is set to grow at a sustained rate through 2022, exhibiting 3.2% CAGR during the 2015-2022 timeframe. Despite all the challenges posed by payers and the increasing scrutiny on the price of new pharmaceuticals, the analysis based on European Drug Forecast data paints a positive outlook for the pharmaceutical industry on the continent.

Figure 1 clearly illustrates the role of new R&D assets in driving market growth whereas among marketed products the uptake of recently launched medicines is expected to offset the decline of key brands due to generic and biosimilar competition.

Figure 1

Total Europe market sales (€bn)

Source: EvaluatePharma® European Drug Forecasts, June 2016



European pharma growth 2015-2022

3.2%

Source: Evaluate's European Drug Forecasts, June 2016.

GDP growth 2015-2022

1.6%

Source: IMF estimates for 2015-2022, June 2016. 2021-2022 Evaluate analysis based on IMF data.

Two factors are at play behind the projected impact of new therapies:

1. A **new stream of potential medical breakthroughs** which are likely to transform many therapy areas. Oncology – driven by the uptake of PD-1/PD-L1 inhibitors (e.g. Opdivo, Keytruda) – is going through a medical revolution that is likely to re-shape the current clinical guidelines. Innovation is not just limited to oncology. Advances are also expected in other fields: Ocrevus (ocrelizumab) in multiple sclerosis, Entresto (valsartan, sacubitril) in chronic heart failure, Praluent (arilumab) and Repatha (evolocumab) in dyslipidemia and baricitinib in rheumatoid arthritis. Even historically challenging areas such as Alzheimer's disease are holding promises with Axovant's intepirdine and Biogen's aducanumab.



2. A **more collaborative environment between pharma manufacturers and European regulators and payers.** The launch of several initiatives at European level – most recently the PRIME (PRiority MEDicine) scheme – aim to strengthen support for medicines that target an unmet medical need and are set to offer a major therapeutic advantage. These are ultimately having the effect of creating a common language between regulators and manufacturers on clinical development protocols. This trend is resulting in greater alignment on the appropriate end points and design criteria for clinical trials, ultimately boosting the productivity of pharmaceutical R&D. Furthermore, it is now an established practice for manufacturers and national governments to have early dialogues around the type of outcomes that need to be demonstrated in order to address payers' requirements for funding.

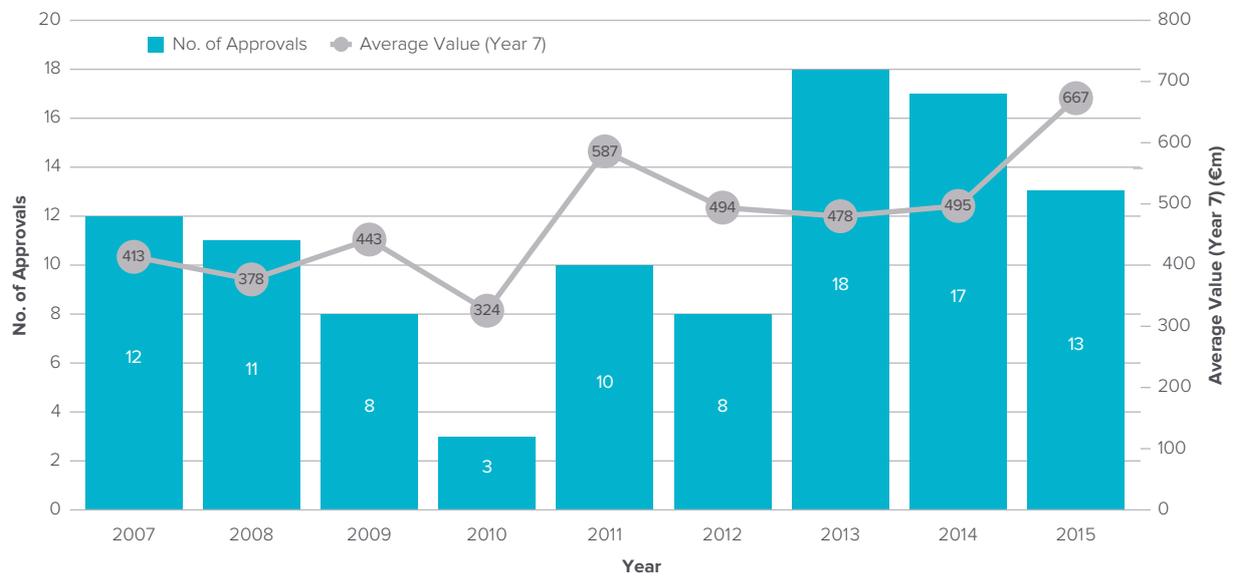
This latter point is also reflected in the data on Figure 2 that shows the number of approvals of top 200 products in Europe (based on 2022 European forecasts) and the average value of the approvals (based on projected/actual sales after 7 years post launch). It is quite apparent that the combination of improved clinical design coupled with medical innovation has led to an increase in the numbers of high value products launched by pharmaceutical companies (which in the context of the European market can be considered as a reasonable proxy to measure payers' willingness to pay for incremental benefits over the standard of care).

Figure 2

Top 200 products in 2022 – EMA approval by year

Source: EvaluatePharma[®] June 2016

Average value (€m) at year 7 post launch*



*For products launched in 2007, 2014 sales data has been used. For products launched in 2015, consensus forecasts in year 7 (2022) have been used.



The recent wave of approvals is set to transform the ranks of the **top selling products in Europe in 2022** (see Figure 3).

In a pharmaceutical industry where the majority of the headlines are focused on oncology, it is somehow surprising to find **Xarelto** at the top of the list, strongly supported by analysts' consensus (worldwide sales in 2022 anticipated at about \$8b) and fuelled by the expected expansion into follow-on indications such as chronic heart failure.

The **hepatitis C storm** will slowly fade away as **Sovaldi** and **Harvoni** will be affected by increasing pricing pressure in addition to a reduction in the number of addressable patients.

Oncology will lead the game with five compounds in the top 10, all of which are coming from recent development activities with the exception of **Herceptin**, which is set to lose ground due to the anticipated launch of biosimilars. In the respiratory area, while some new innovations are slowly surfacing (e.g. GSK's Nucala), generic competition will force the respiratory blockbusters – **Spiriva** and **Seretide/Advair** – out of the top selling elite.

Figure 3

Source: EvaluatePharma¹ European Drug Forecasts, June 2016

Top Selling Products in Europe 2015 v 2022

Rank	Top Products 2015	Product Sales 2015 (€bn)		Top Products 2022	Product Sales 2022 (€bn)
1	Humira	3.3		Xarelto	2.6
2	Enbrel	2.1		Opdivo	2.4
3	Herceptin	2.1		Revlimid	2.0
4	Harvoni	2.0		Eylea	1.7
5	Rituxan	1.9		Perjeta	1.6
6	Avastin	1.9		Soliris	1.6
7	Seretide/Advair	1.5		Xtandi	1.5
8	Sovaldi	1.4		Humira	1.5
9	Spiriva	1.4		Herceptin	1.4
10	Lucentis	1.4		Tecfidera	1.2



A closer look at some of the key therapy area dynamics

Oncology

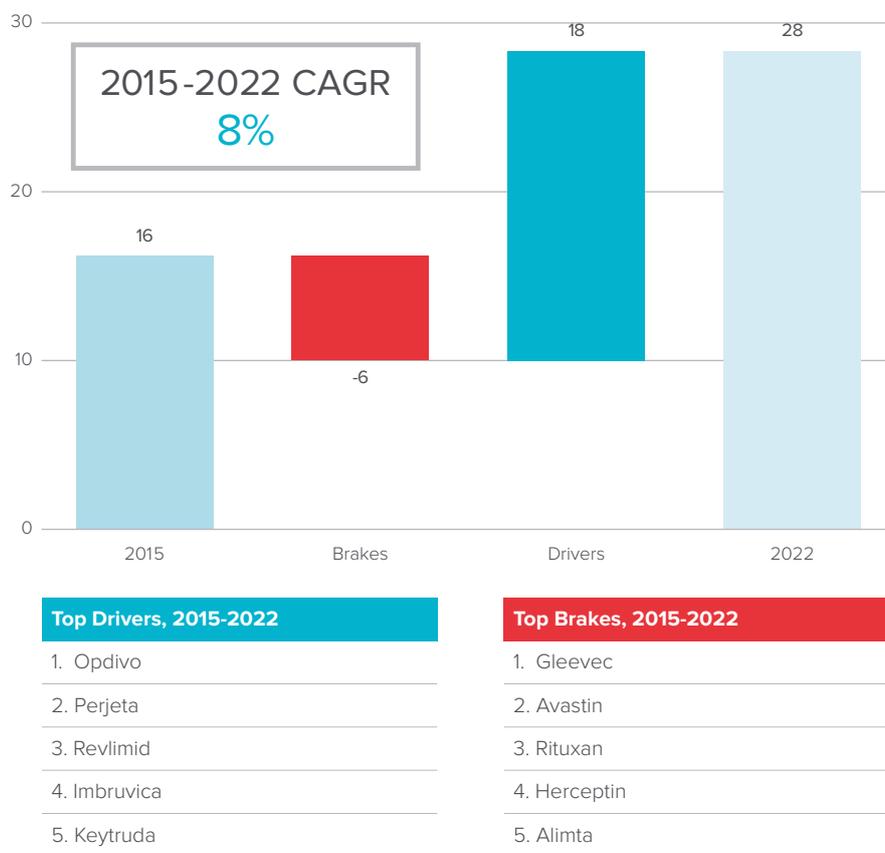
The rise of potential breakthrough medications in oncology have accelerated significantly over the past three years with the launch of the first immuno-oncology treatments Opdivo and Keytruda with new promising assets slowly emerging on the horizon such as Roche’s Tecentriq. In the hematology arena, Revlimid and Imbruvica are set to lead the game, despite the latter having a recent set back with UK’s NICE for approval in chronic lymphocytic leukaemia (yet, the drug is still accessible via England’s Cancer Drug Fund). Overall the market is expected to grow at an average annual rate of 8% (see Figure 4).

The funding of these new therapies will remain one of the most pressing challenges facing payers given their use in combination with existing therapies hence doubling – and in some cases tripling – the total cost of therapy. A potential help for payers may come from the expected introduction of biosimilars (Herceptin, Rituxan and Avastin) and generics (Gleevec). However this is likely to prove a challenging battleground for biosimilar players, in particular against Herceptin (trastuzumab) where Roche has deployed a robust lifecycle management strategy with the launch of Perjeta, Kadcyla and the subcutaneous version of Herceptin.

Figure 4

European Oncology Market 2015-2022 (€bn)

Source: EvaluatePharma® European Drug Forecasts, June 2016



Brakes = Decline 2022 vs. 2015, Drivers = Growth 2022 vs. 2015



Diabetes

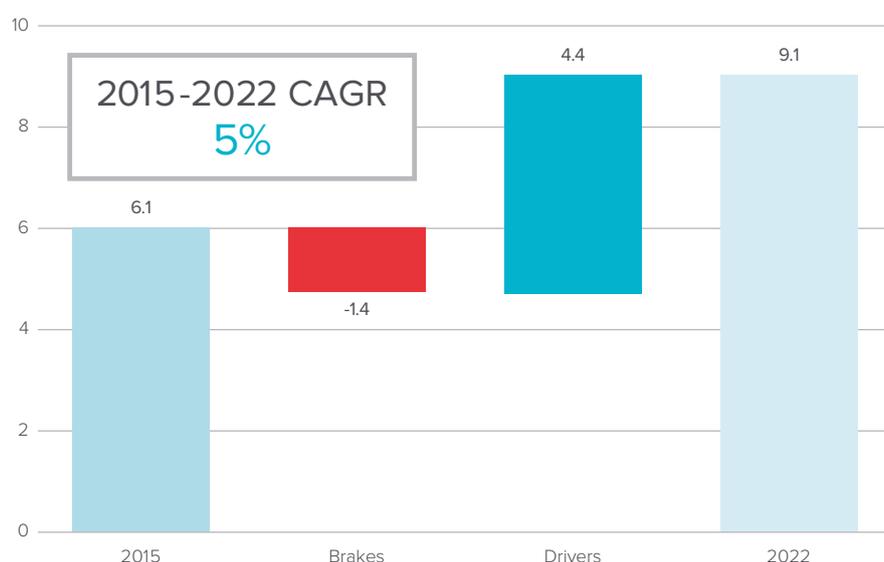
The diabetes market is anticipated to grow at an annual rate of 5% (See Figure 5) led by Novo Nordisk’s portfolio where Xultophy – a combination of liraglutide (Victoza) and insulin degludec (Tresiba) – is expected to generate the largest contribution to sales growth along with its single ingredients and the upcoming once-weekly GLP-1 therapy semaglutide. Boehringer Ingelheim’s and Lilly’s Jardiance (empagliflozin) – despite being the third SGLT2 to hit the market (after Farxiga and Invokana) – is anticipated to be the best-in-class products in this space based on the recent release of promising top-line clinical data.

The overall growth of the diabetes market will be partly affected by the launch of biosimilar insulins, with Lantus expected to lose ground through 2022 (Abasaglar approved by EMA in October 2014).

Figure 5

European Diabetes Market 2015-2022 (€bn)

Source: EvaluatePharma® European Drug Forecasts, June 2016



Top Drivers, 2015-2022

1. Xultophy
2. Jardiance
3. Victoza
4. Tresiba
5. Semaglutide

Top Brakes, 2015-2022

1. Lantus
2. Humalog
3. NovoRapid
4. Levemir
5. NovoMix30

Brakes = Decline 2022 vs. 2015, **Drivers** = Growth 2022 vs. 2015



Immunology*

*Focus on anti-TNF market and novel mechanisms of action active in the same space (e.g. JAK-1/2, IL-17)

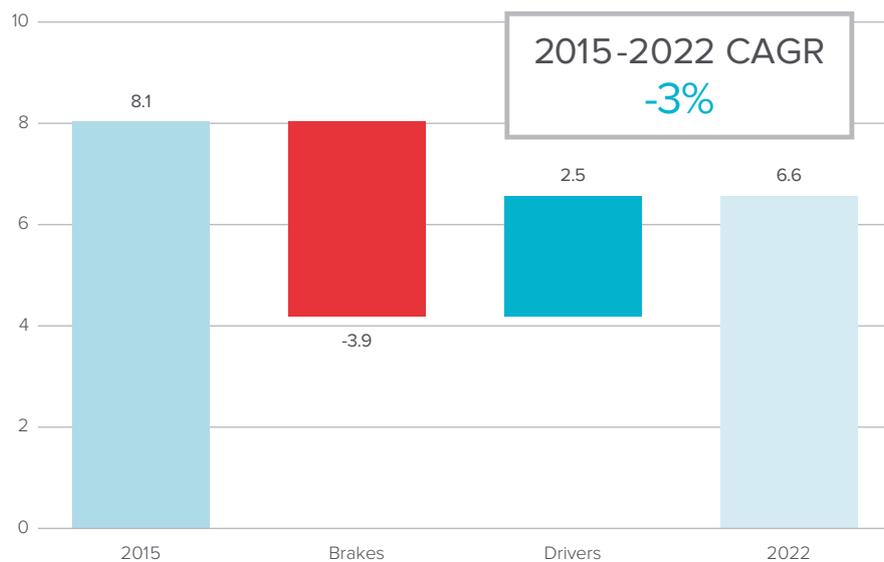
The market outlook in the anti-TNF space has been affected by the recent introduction of the first biosimilar therapies, widely awaited by payers who see this area as potentially yielding significant savings. Biosimilar versions of Remicade (Remsima/Inflectra) have been around for longer than a year and now Enbrel is under scrutiny following the approval of Benepali (etanercept biosimilar). The situation for Humira is less certain as an important patent litigation is currently ongoing that could ultimately keep biosimilars of the biggest selling drug in the world out of the market until 2022 (hence enabling Humira to keep the market leadership and most likely the European leadership).

Even if biosimilars don't hit the market during the 2015-2022 timeframe, a potentially adverse event to Humira and the other anti-TNF therapies may come from new innovations, such as Lilly's baricitinib and Novartis' Cosentyx. The former in particular has recently released impressive top-line data signalling potential superiority versus market leader Humira.

Figure 6

European Immunology Market 2015-2022 (€bn)

Source: EvaluatePharma® European Drug Forecasts, June 2016



Top Drivers, 2015-2022

1. Cosentyx
2. Baricitinib
3. Otezla
4. ABP-501 (Adalimumab)
5. Multistem

Top Brakes, 2015-2022

1. Humira
2. Enbrel
3. Remicade
4. Simponi
5. Orencia

Brakes = Decline 2022 vs. 2015, **Drivers** = Growth 2022 vs. 2015

*Immunology includes therapy areas such as Rheumatoid Arthritis, Psoriasis, Crohn's disease, ... (includes anti-TNFα, JAK-1, ...)



Conclusions:

Are healthcare systems and payers ready for innovation?

The pharmaceutical industry has been going through a period of radical transformation of its business model which, coupled with scientific advances, is now resulting in a new wave of innovative treatment options that are anticipated to put additional pressure on the financial resources of already cash-strapped healthcare systems.

If in the past the balance was primarily achieved via price-cutting policies either supported by the introduction of cheaper generic or biosimilar versions, forced rebates at national level or the application of international reference pricing rules, such a trend is no longer sustainable. It is probably time for payers and the pharmaceutical industry to work together at the same table and devise new and more efficient funding methods as opposed to the often theoretical risk-sharing and pay-for-performance schemes that have been trialled so far.

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- Map future trends of key marketed drugs

R&D Horizon Scanning

- Forecasts for 500+ R&D products
- Map key pipeline assets likely to launch by 2022 and measure impact

Market Assessment

- Historical government and company reported sales data (EU 5 & key markets)
- Compare product performance across key European markets

Pricing Comparison Analysis Across Countries

- Government reported pricing and volume analysis (EU 5 & key markets)
- Perform comparative analysis of prices across EU countries



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