The Impact of Biosimilar Competition in Europe 2022

Prepared for European Commission (DG SANTE)

Per Troein, *VP, Strategic Partners*
Max Newton, *Global Supplier & Association Relations*

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Disclaimer:

This report has been prepared by IQVIA at the request of the European Commission services with initial contributions on defining the KPIs from EFPIA, Medicines for Europe, and EuropaBio.

The observations have been developed solely by IQVIA based on the data and analyses performed. The information and views set out in this report are those of its authors and are not to be attributed to, nor necessarily reflect the views of the European Commission or any of its services.

The European Medicines Agency (EMA) has a central role in setting the rules for biosimilar submissions, approving applications, establishing approved indications and monitoring adverse events, and if necessary, issuing safety warnings. We have, when appropriate, quoted their information and statements.

Agenda

+ **Introduction**
+ Methodology and the Country & Therapy Area KPIs
+ IQVIA's 5 Observations in 2022
+ *10.10am – 10.20am:* Q&A session

The analysis builds on historic publications on biosimilars

Key observations on price, volume and market share since the arrival of biosimilars in Europe

2015

Competition drives down price

The correlation between biosimilars market share and price reduction is weak

Competition can also influence the originator's behaviours

Lower prices has the most impact on usage (patient access) in countries with low initial usage

The product profile differences in classes can explain differences in impact on the KPIs

2016

Competition drives down price

The correlation between biosimilars market share and price reduction is weak

Competition can also influence the originator's behaviours

Lower prices increase patient access in countries with low initial usage

The product profile differences in classes can explain differences in impact on the KPIs

2017

The entrance of biosimilars increases price competition

In some therapeutic classes, lowering the price of the referenced product can limit the market penetration of the biosimilar

There is a first to market advantage in biosimilar markets

Biosimilars have the potential to improve patient access of the total market

2018

The entrance of biosimilars increases price competition

Biosimilars have the potential to improve patient access of the total market

In some countries, biosimilars have completely taken over

In some therapeutic classes, lowering the price of the referenced product can limit the market penetration of the biosimilar

The speed of uptake has increased for some of the more recent biosimilar launches

2019

Biosimilar competition has a significant potential impact on overall drug spend

Major products see fast uptake and large price reductions

Originator manufacturers have changed strategy to stay competitive

Access is not yet increasing for all molecules and in all countries after biosimilar introduction

More is needed to create a sustainable market for biosimilar manufacturers

2020

Biosimilar competition continues to offer opportunities to make healthcare savings

Some countries are not increasing usage despite price reductions

The variation of originator response to protection expiry

Several models can work to support competitive markets

The real impact of biosimilar competition is just beginning

2021

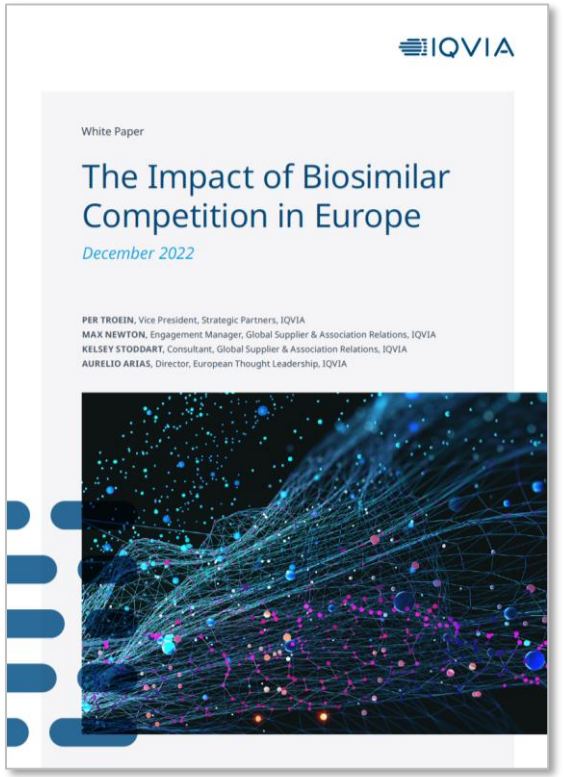
The pandemic has impacted certain segments of the biologic market

The savings from biosimilar competition reach an all-time high

Development of access to biologic medicines remains challenging

The competition environment in Europe is changing

Ensuring preparedness for the future of biosimilar opportunity



Sources: IQVIA/IMS Health, The Impact of Biosimilar competition in Europe (2015-2021)
The Impact of Biosimilar Competition in Europe 2022; Prepared for European Commission (DG SANTE) December 2022

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+ Q&A

9 therapy classes with biosimilar competition are shown

The products are split into 4 categories based on regulatory and protection status

Therapy classes

1. **Human Growth Hormone** (HGH)
2. **Granulocyte-colony Stimulating Factor** (GCSFs)
3. **Epoetin** (EPO)
4. **Anti-Tumour Necrosis Factor** (Anti-TNFs)
5. **Fertility** (Follitropin Alfa)
6. **Insulins**
7. **Oncology**
8. **Low-Molecular-Weight Heparin** (LMWHs)
   Shown in for the 1st time in 2021
9. **Ophthalmology**
   Shown in anticipation of biosimilar entry

Product categorisation

Description	Key	Other segmentation	
• **Biosimilar Medicinal Product**: Product, granted regulatory approval, demonstrating similarity to the Reference Medicinal Product in terms of quality characteristics, biological activity, safety and efficacy.		**Accessible** market	**Total market:** products within the same ATC3**
• **Referenced Medicinal Product:** Original product, granted market exclusivity at the start of its life, exclusivity has now expired, and the product has been categorised as referenced by having a biosimilar with an EMA-approved marketing authorisation available on a European market.			
• **Non-Referenced Medicinal Product**: Original product, granted market exclusivity at the start of its life, exclusivity has now expired*, and the product has never been categorised as a Referenced Medicinal product by receiving EMA-approved marketing authorisation.			
• **Non-accessible category**: products within the same ATC4 code as the accessible category products. These are typically second-generation products; this category may include products with different dosing schedules and / or route of administration to those in the accessible category, **and** have valid protection status		**Non-accessible** market	

**The Intellectual Property for biologicals can involve multiple patents and patent timelines for each individual product and therefore it is difficult to given an exact date for patent expiry for biologicals. It should be noted that these results are estimates as determined from IQVIA MIDAS and ARK Patent Intelligence where available.* ** ATC definitions: EPO = B3C0 (ERYTHROPOIETIN PRODUCTS); GCSFs = L3A1 (COLONY-STIMULATING FACT.); HGH = H4C0 (GROWTH HORMONES); ANTI-TNF = L4B0 (ANTI-TNF PRODUCTS); INSULIN = A10C 1,2,4,5,9; Oncology = L1G0 1,2,3,5,9 (RESTRICTED TO 3 major products with biosimilar competition); LMWHs = B1B2 (FRACTIONATED HEPARINS), Ophthalmology: S1PO (OCULAR ANTINEOVAS)

The report is continually adjusted to reflect new situations

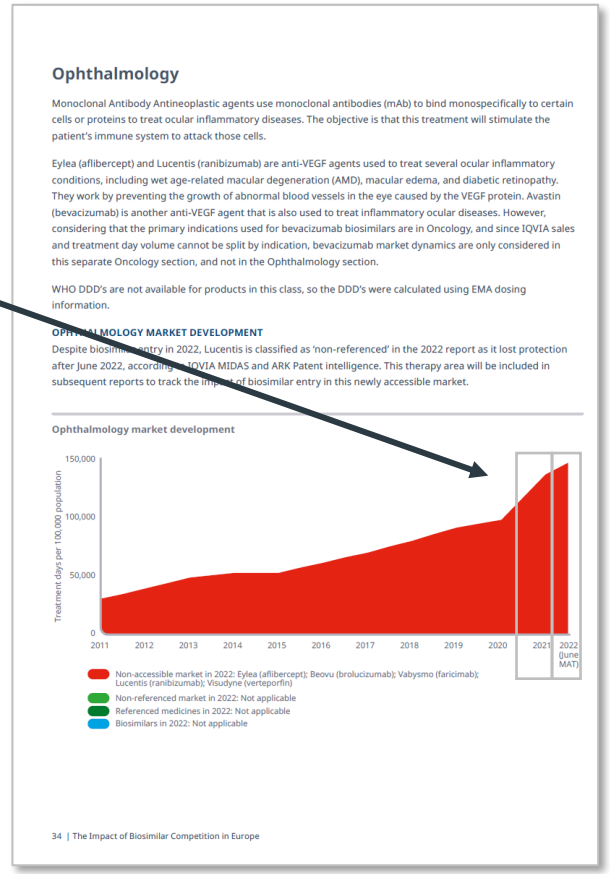
Information for biosimilar stakeholders

Expanded data period

- In 2022, full-year 2022 data **plus** June MAT 2022 data to remain up to date

Stricter definitions

- Restricting the definition of ‘referenced’ to reflect biosimilar EMA-MA prior to LOE
- Protection status was not explicitly highlighted
- Historic recategorization



Ophthalmology

Monoclonal Antibody Antineoplastic agents use monoclonal antibodies (mAb) to bind monospecifically to certain cells or proteins to treat ocular inflammatory diseases. The objective is that this treatment will stimulate the patient's immune system to attack those cells.

Eylea (aflibercept) and Lucentis (ranibizumab) are anti-VEGF agents used to treat several ocular inflammatory conditions, including wet age-related macular degeneration (AMD), macular edema, and diabetic retinopathy. They work by preventing the growth of abnormal blood vessels in the eye caused by the VEGF protein. Avastin (bevacizumab) is another anti-VEGF agent that is also used to treat inflammatory ocular diseases. However, considering that the primary indications used for bevacizumab biosimilars are in Oncology, and since IQVIA sales and treatment day volume cannot be split by indication, bevacizumab market dynamics are only considered in this separate Oncology section, and not in the Ophthalmology section.

WHO DDD's are not available for products in this class, so the DDD's were calculated using EMA dosing information.

OPHTHALMOLOGY MARKET DEVELOPMENT

Despite biosimilar entry in 2022, Lucentis is classified as ‘non-referenced’ in the 2022 report as it lost protection after June 2022, according to IQVIA MIDAS and ARK Patent intelligence. This therapy area will be included in subsequent reports to track the impact of biosimilar entry in this newly accessible market.

Ophthalmology market development

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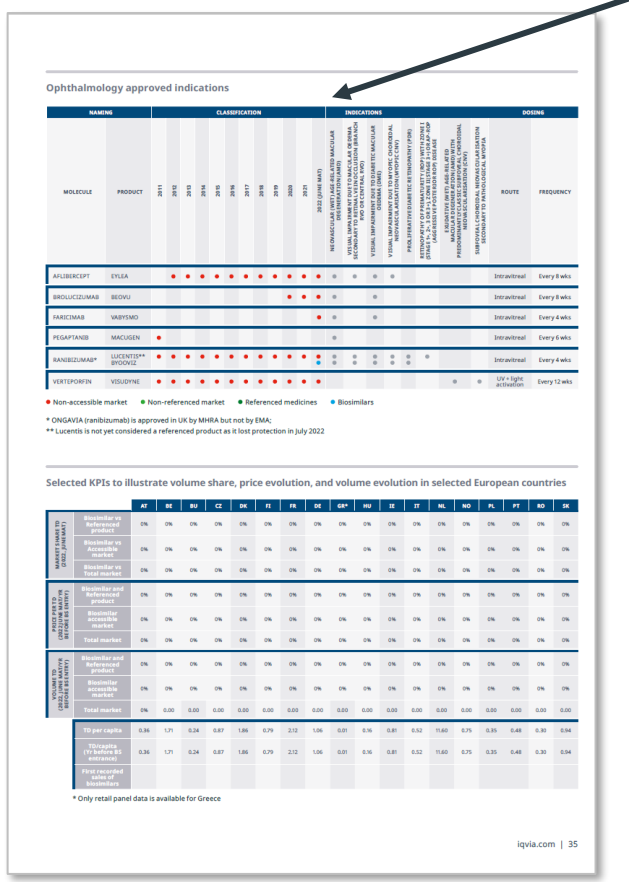

Ophthalmology approved indications

MOLECULE	PRODUCT	ROUTE	FREQUENCY
AFLIBERCEPT	EYLEA	Intravitreal	Every 8 wks
BROLUCIZUMAB	BEOVU	Intravitreal	Every 8 wks
FARICIMAB	VABYSMO	Intravitreal	Every 4 wks
PEGAPTANIB	MACUGEN	Intravitreal	Every 6 wks
RANIBIZUMAB*	LUCENTIS** / BYOOVIZ	Intravitreal	Every 4 wks
VERTEPORFIN	VISUDYNE	UV + light activation	Every 12 wks

● Non-accessible market ● Non-referenced market ● Referenced medicines ● Biosimilars

* ONGAVIA (ranibizumab) is approved in UK by MHRA but not by EMA;
** Lucentis is not yet considered a referenced product as it lost protection in July 2022

Selected KPIs to illustrate volume share, price evolution, and volume evolution in selected European countries

		AT	BE	BU	CZ	DK	FI	FR	DE	GR*	HU	IE	IT	NL	NO	PL	PT	RO	SK
MARKET SHARE TO BIOSIMILAR (2022 Q4 MAT)	Biosimilar vs Referenced product	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar vs Accessible market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar vs Total market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
PRICE EVOLUTION (2022 Q4 MAT) VS. BIOSIMILAR ENTRY	Biosimilar and Referenced product	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar accessible market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Total market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
VOLUME EVOLUTION (2022 Q4 MAT) VS. BIOSIMILAR ENTRY	Biosimilar and Referenced product	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Biosimilar accessible market	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
	Total market	0%	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
TD per capita		0.36	1.71	0.24	0.87	1.86	0.79	2.12	1.06	0.01	0.16	0.81	0.52	11.60	0.75	0.35	0.48	0.30	0.94
Thiopatta (Yr before BS entrance)		0.36	1.71	0.24	0.87	1.86	0.79	2.12	1.06	0.01	0.16	0.81	0.52	11.60	0.75	0.35	0.48	0.30	0.94
First recorded sales of biosimilars																			

* Only retail panel data is available for Greece

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Granularity

- View historical status of products
- Delay to biosimilar entry
- Visibility to 2nd, 3rd, 4th... 12-year history of the market

Larger scope

- Ophthalmology included in full for the first time
- Oncology has been expanded further from rituximab, bevacizumab, and trastuzumab to include (currently) non-accessible biologics pertuzumab and combinations

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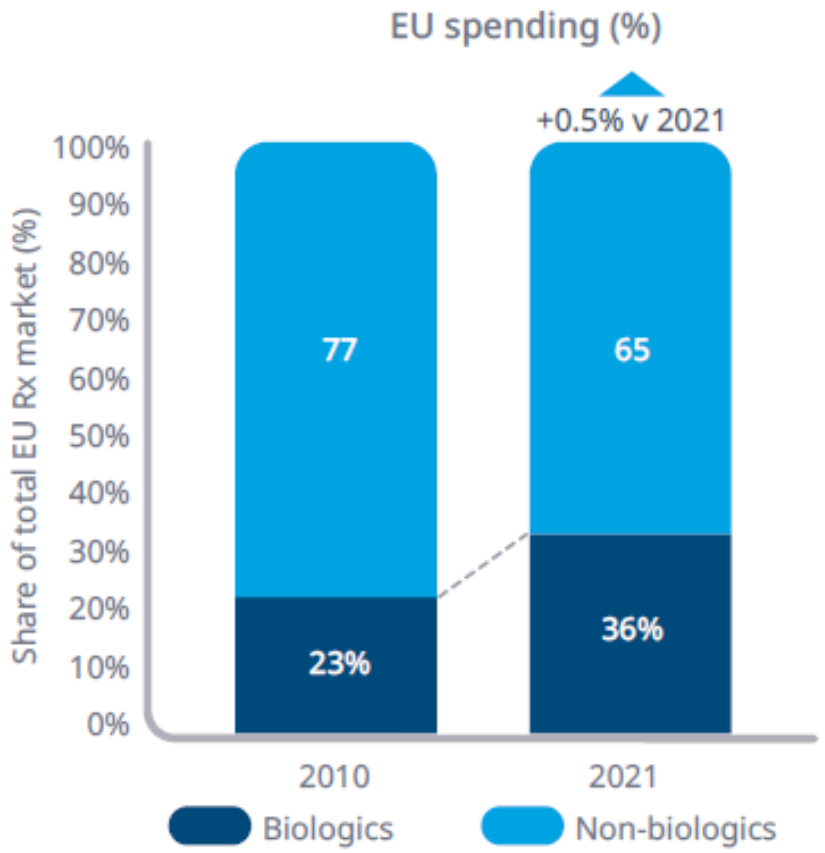
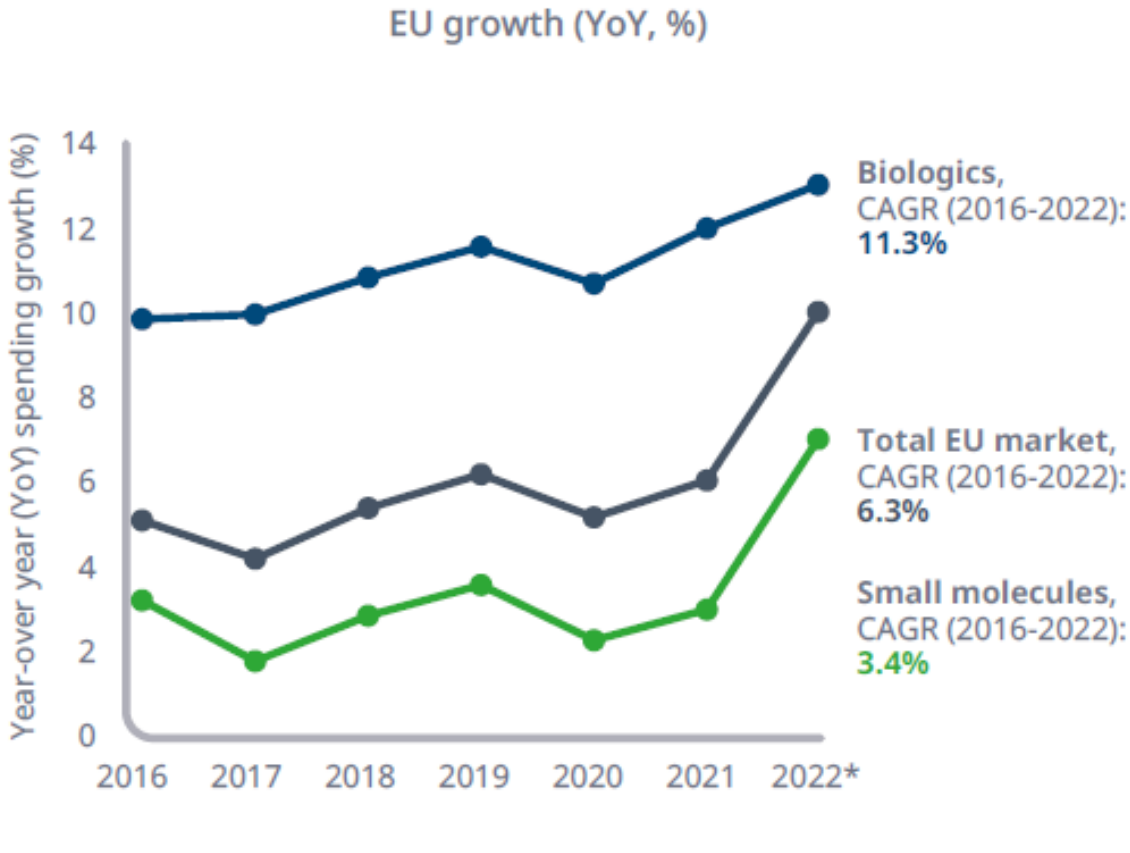
The biologic market is increasingly important

Biologics represent a large portion of current expenditure, making competition critical

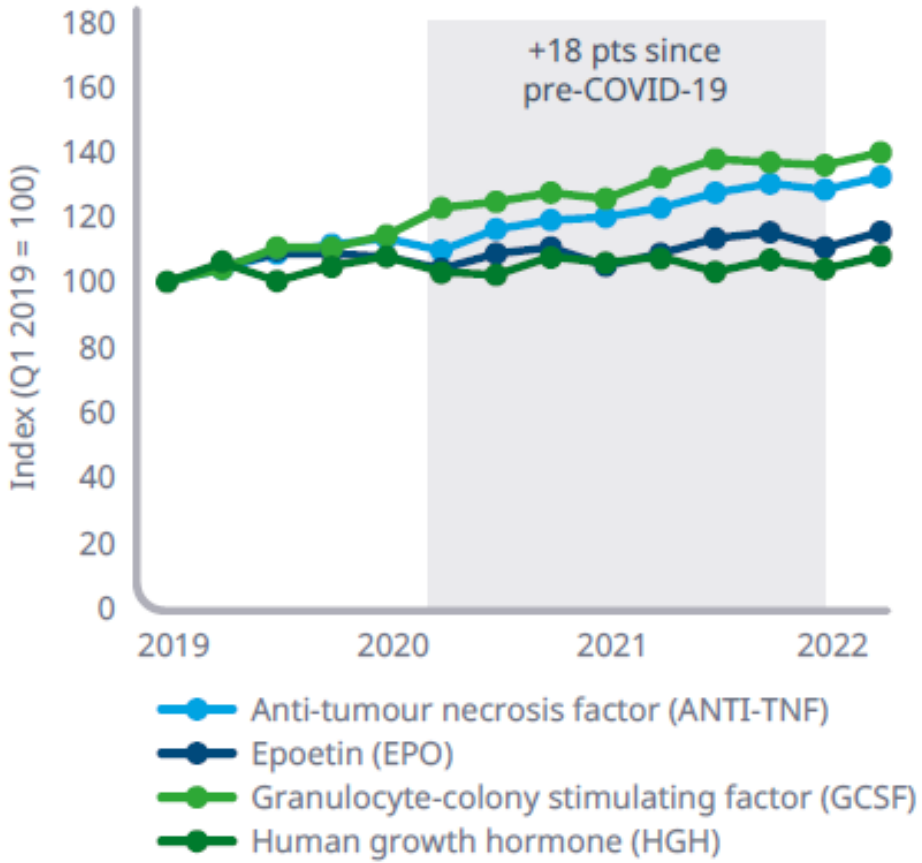


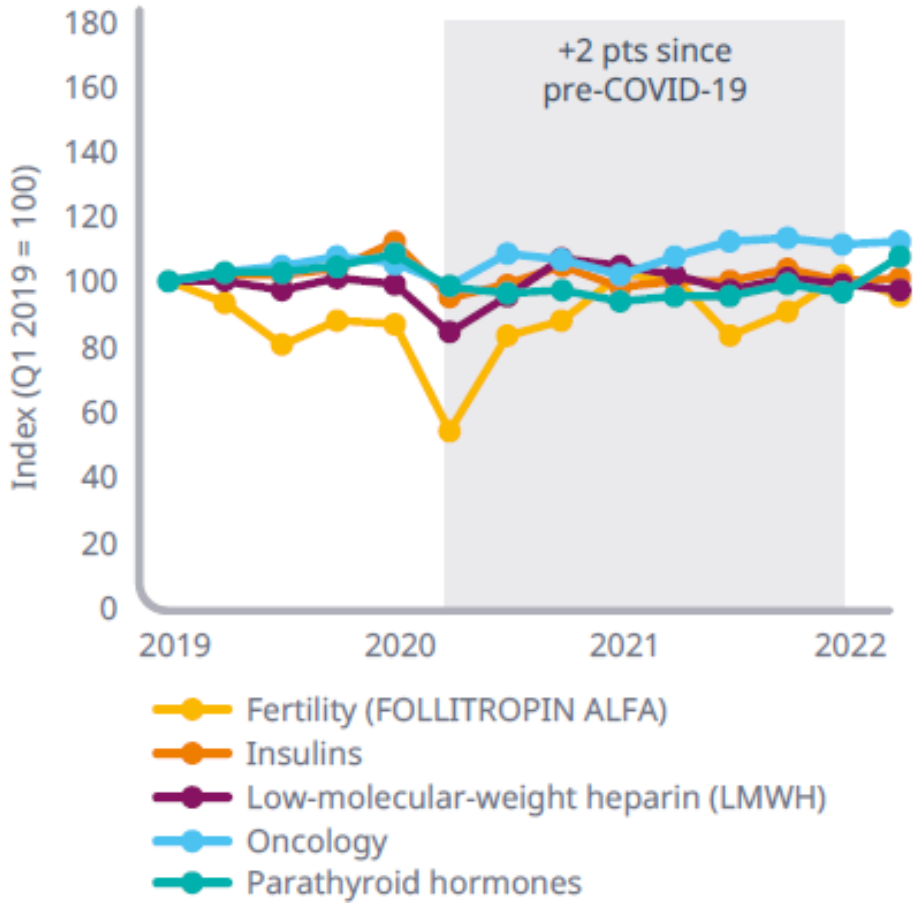


*H2 MAT 2022
Notes: Biologic market includes originator biologics and biosimilars; and EU country scope (excludes UK, Switzerland)
Source: IQVIA MIDAS (Q2 2022), Rx only; Biologic molecules exclude ATC-V (vaccines, and various)

The direct impact of COVID-19 has largely passed

Indirect impact on access to healthcare, diagnosis, and treatments are being minimised

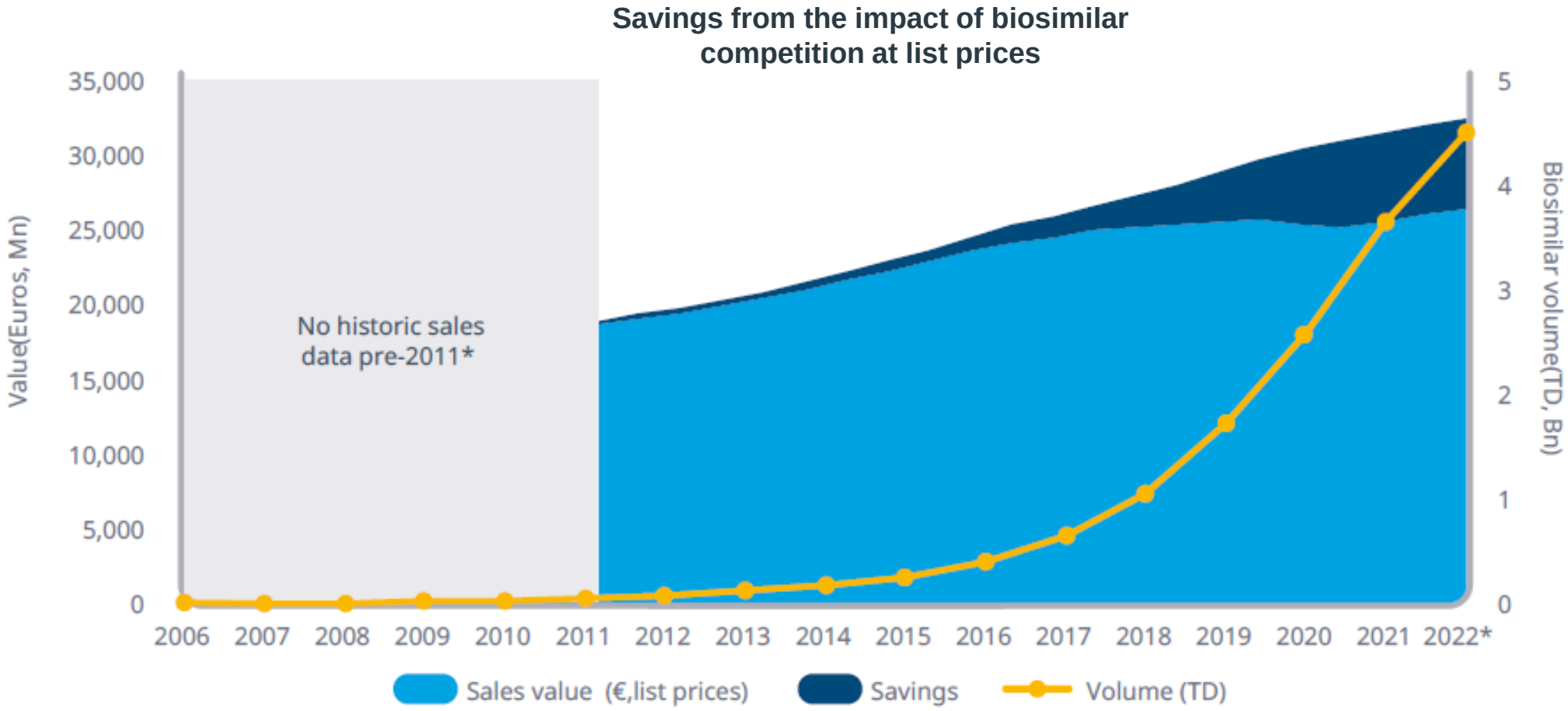




Notes: Ophthalmology therapy area excluded due to the impact of new product entries within the class skewing the index

EU savings from the impact of competition have reached >€30Bn

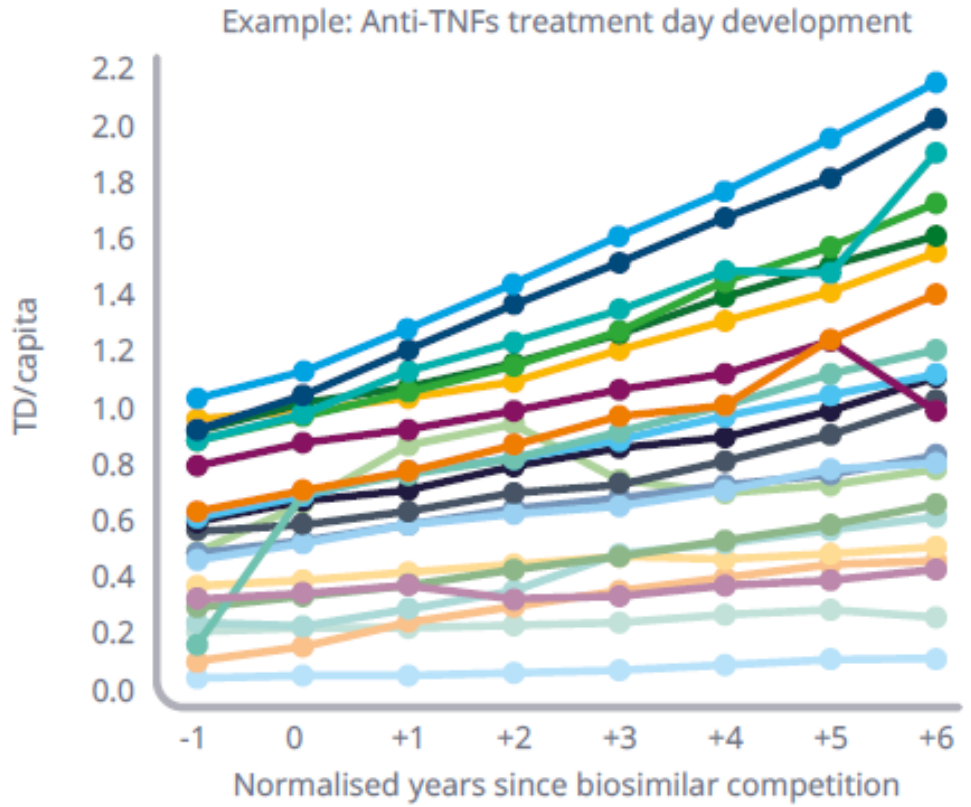
Cost has fallen for multiple years in a row while total volume has increased



Caveats: This figure is not equivalent to all savings. And is therefore an under-estimate. The data does not include the impact of rebates or discounts, which may have been present prior to the introduction of biosimilars in small quantities, and are highly significant post-biosimilar entry as it is based on publicly available list prices.. Source: IQVIA MIDAS™ data from 2006 – 2022, using Euros at constant exchange rates; value includes all originator products with approved biosimilars from 2006 – 2022, covering the full European Economic Area (33 CTYs), calculated volume is in treatment days determined by WHO-DDD, and where values are unavailable via Oncology Dynamics Physician Survey (2017) DDD estimates. Volume is solely biosimilar treatment days

Access to biologics is increasing in all country, but not evenly

Countries which high growth start from a low base and are not catching up



	% growth (7 year CAGR)	Abs growth
Norway	11%	1.12
Ireland	12%	1.10
Sweden	10%	0.84
Belgium	8%	0.69
Denmark	12%	1.02
Netherlands	7%	0.59
Finland	12%	0.77
Switzerland	3%	0.20
Austria	33%	1.05
France	9%	0.51
UK	9%	0.51
Spain	9%	0.47
Slovenia	8%	0.34
Germany	8%	0.35
Slovakia	7%	0.29
Portugal	12%	0.37
Czech	15%	0.38
Italy	5%	0.14
Bulgaria	24%	0.35
Hungary	4%	0.11
Romania	3%	0.05
Poland	15%	0.07

Notes: Calculation is based on the normalized year before biosimilar entry for each molecule in the anti-TNF class, and the treatment days before and since the LOE date in Europe

The disparity between countries is increasing

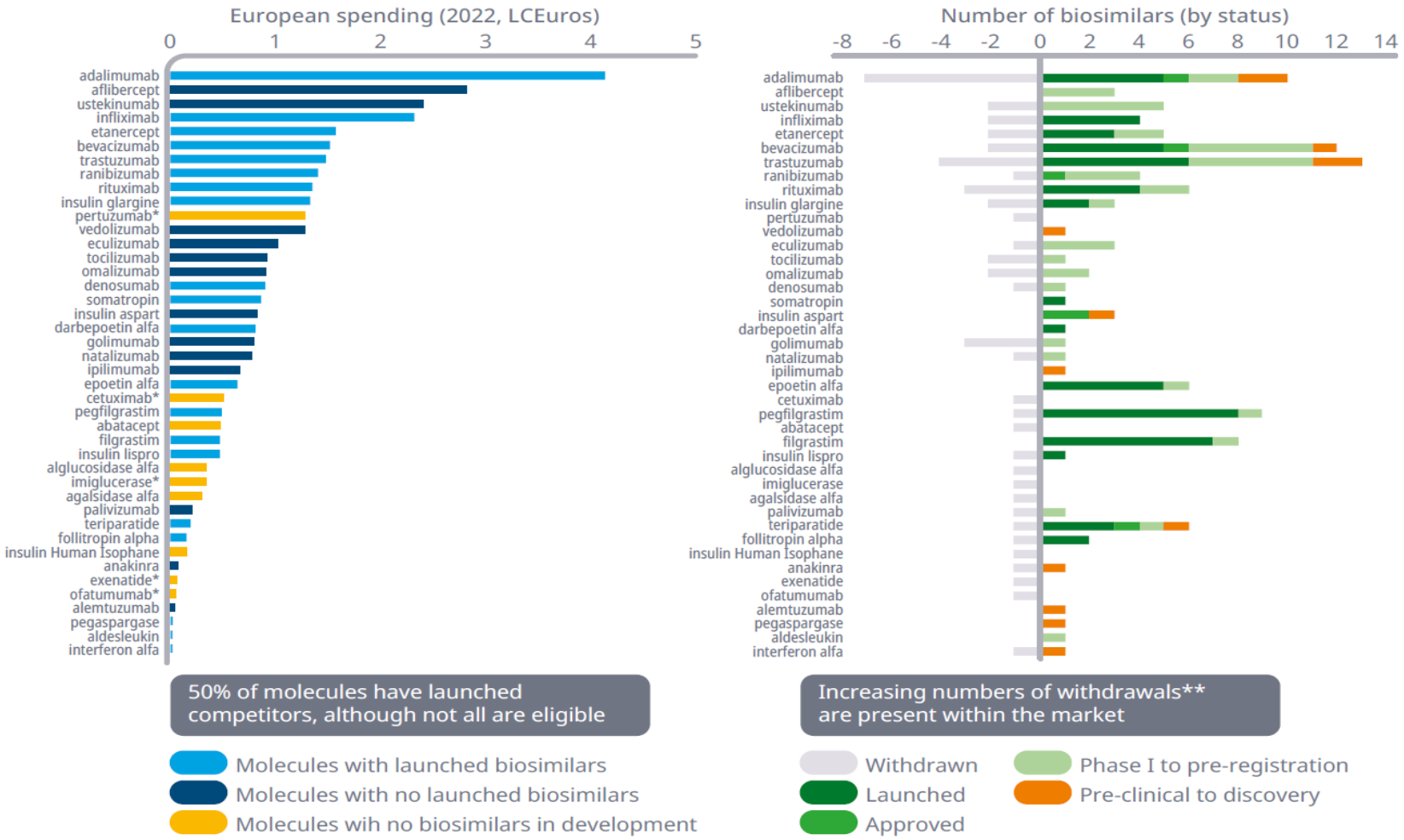
Increasing the uptake of biosimilars is not enough to reduce the gap without considering the system

*Normalised to the year of first recorded biosimilar sales in each country, to account for markets that are delayed in using biosimilars after loss of patent protection

Chart notes: Includes TD for all market segments (Non-accessible, Non-referenced, Referenced, Biosimilars); All countries are ranked based on TD/Capita at +6 years and the top-5 and bottom-5 countries includes in this analysis

High proportions of EU spending expect competitors

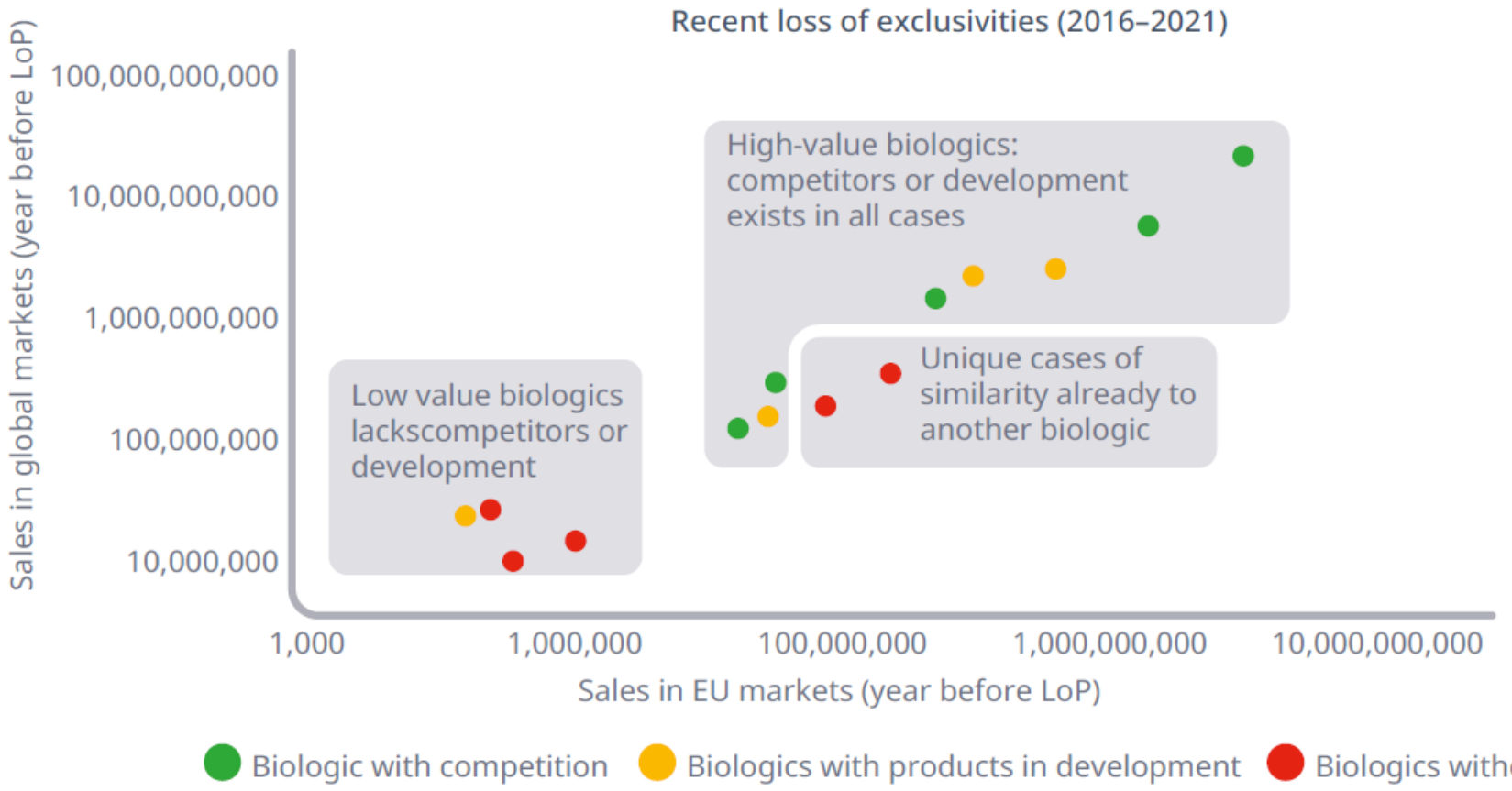
Competition within the major molecules is increasingly fierce



Source: IQVIA Institute, The Global Use of Medicines 2022, Outlook to 2026 (January 2022). Notes: * Molecules for which no biosimilar development has been reported in last 3 years; **Withdrawals = pipeline withdrawals or discontinuations

Not all molecules are attractive for competitors to enter

Biologic molecules do not necessarily support a biosimilar in the current system

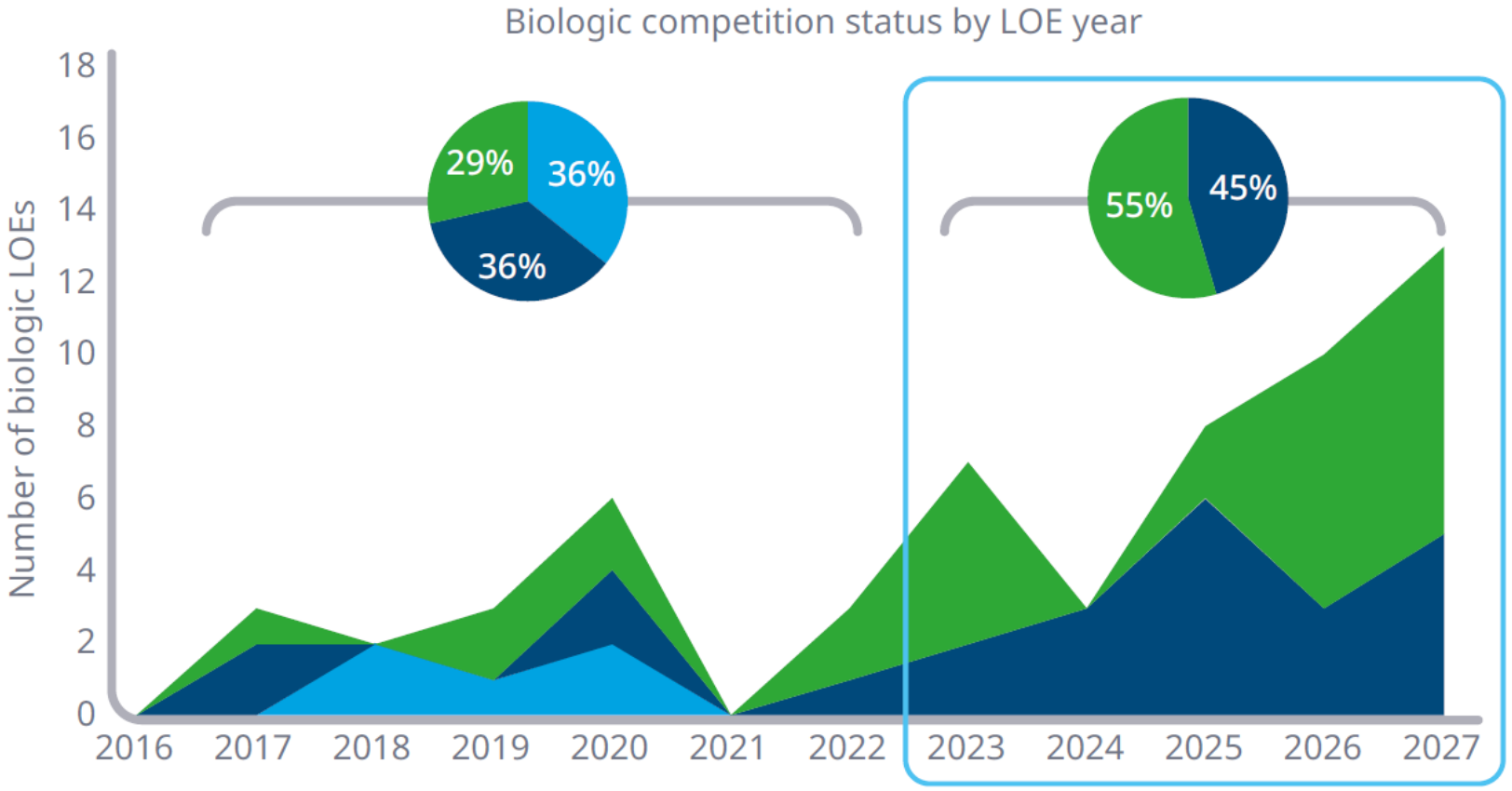


- Molecules (especially OMPs) may not support multiple competitors at significantly reduced prices
- Products with low sales values are unattractive to biosimilar manufacturers due to the cost of comparators, and development
- Some biologics in this analysis are defined as 'very similar' or 'very slightly different' by the EMA to other biologics and are therefore unlikely to require their own unique biosimilar

Source: IQVIA Institute, Protection Expiry and Journey into the Market: Pharmaceutical products in Europe (September 2022) https://www.iqvia.com/insights/the-iqvia-institute/reports/protection-expiry-and-journey-into-the-market

Biologic LOEs are increasing, and research has already started

The number of molecules is higher, while average value is lower

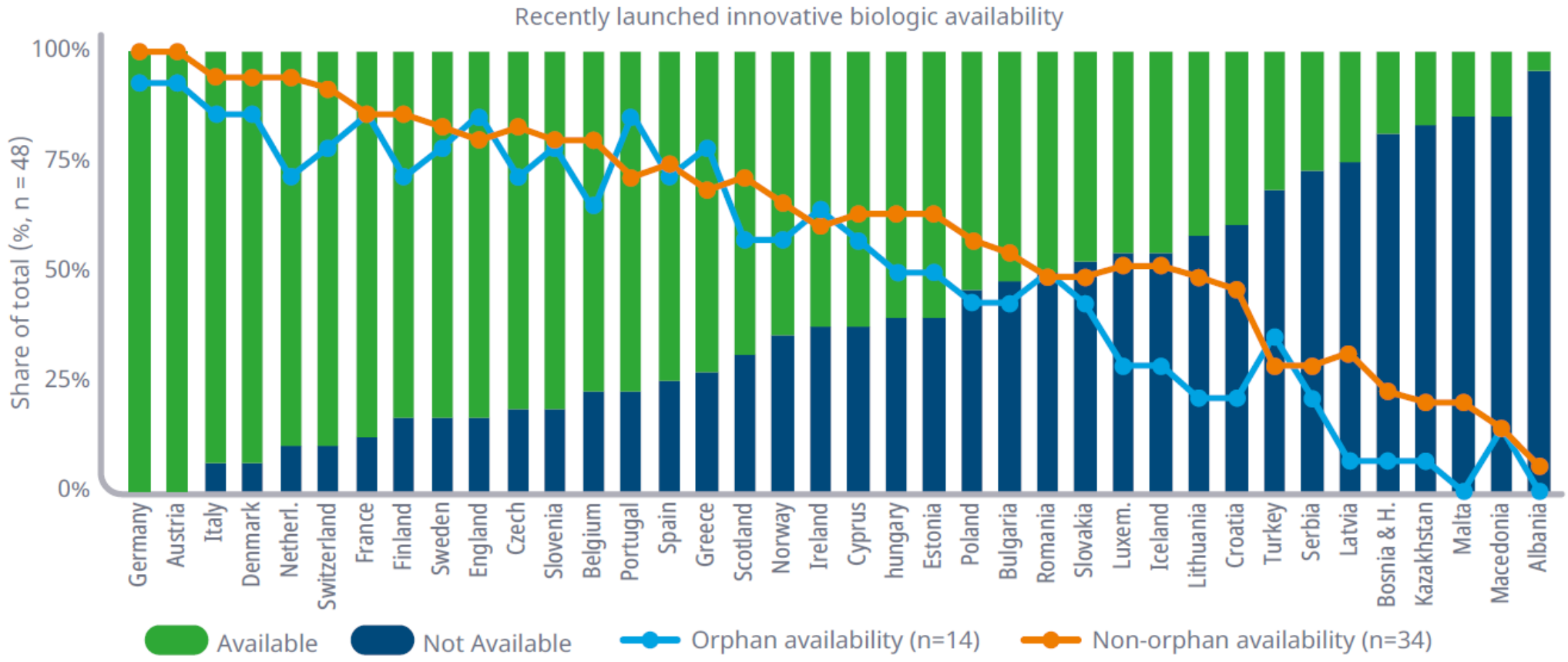


- 2/3 of historic LOEs received biosimilar competition, due to molecule size and type
- More biologics will be losing protection that historically (+30)
- More biologics molecules have a competitor in development than before (+14)
- Not all future biologics will have competition, historically this has been ~1/3 of all molecules
- Multiple high value biologics losing exclusivity which explains the uptick in 2025
- Biologics with competitors development are already for products losing exclusivity in 2027

Source: IQVIA Patent Intelligence, Pipeline Intelligence, and IQVIA Forecast Link analysis (November 2022); Historic analysis sourced from IQVIA Institute report, Protection expiry and Journey into the Market (2022) Note: The intellectual property for biologicals can involve multiple patents, patent timelines, data exclusivity, and litigation for each individual product and therefore it is difficult to give an exact date for protection expiry for biologicals. It should be noted that these results are estimates as determined from IQVIA MIDAS® and ARK Patent Intelligence where available, and historical products are cross-referenced to public sources

Availability of recently launched biologics is low

Biosimilar entry is complex without originator access, and offers payers limited savings if unused



Source: Based on IQVIA W.A.I.T dataset and IQVIA HTA-Accelerator datasets covering novel active substances (NAS) molecules launched within 2014 – 2020 (November 2022 analysis), including all current EU members, EEA members, and countries considering ascension. Reimbursement defined by availability on a public reimbursement list in a country

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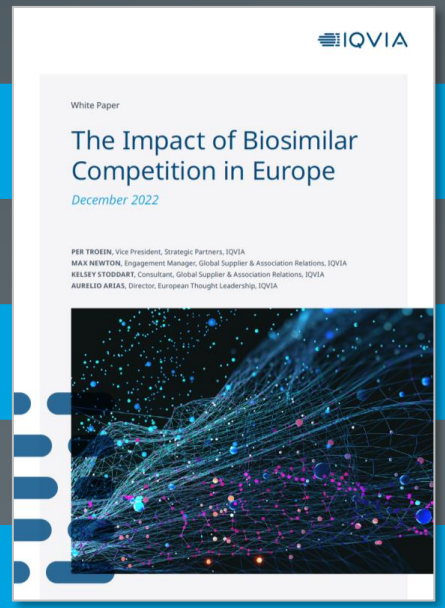
Thank you!

Contact us for further questions

Per Troein (*per.troein@iqvia.com*)
Max Newton (*maximilian.newton@iqvia.com*)



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