The Business of Biosimilars

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Perspectives on the evolving biosimilars landscape

Doug Long

Vice President Industry Relations

March 2015

Agenda

- **The Global Biologic Market**
  - The increasing importance of biologics
  - LoE driving interest and investment
  - Biosimilars gradually emerging

- **Learning from the biosimilar experience**
  - Countless variations: therapy area, country and molecule level
  - What really drives Biosimilars uptake
  - Understanding the role of 2nd generation products
  - Next wave of Biosimilars

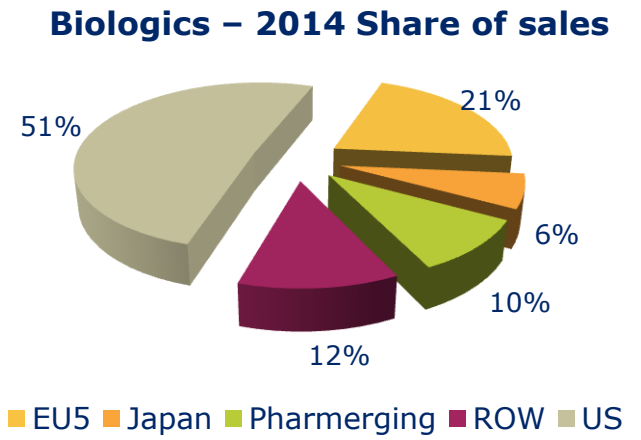
- **Looking ahead**
  - Key biologic areas and biosimilar's targets
  - Originator strategies
  - The trade-off between access and innovation

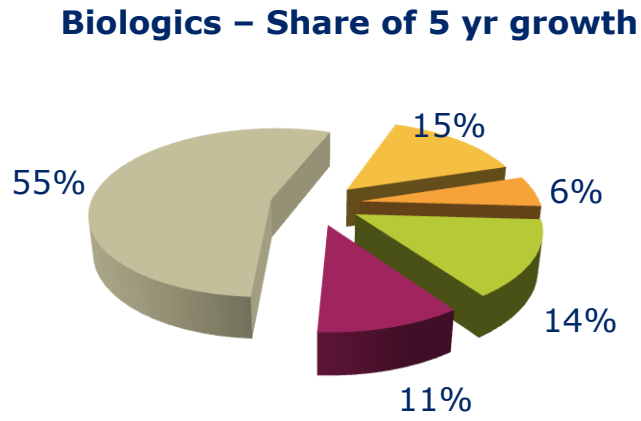
A word on the data used in this presentation

- IMS Health historic and forecast data is presented at list price value
- This excludes rebates and discounts, which can vary across countries, products and over time
- We are very aware of this challenge, but at the moment, when a market-level view is taken of pharmaceutical sales, there is no good quality, consistent substitute for list price level data

Biologics growth continues to outstrip total pharma, showing a steep increase on 2013

Such a trend is putting additional financial pressure on healthcare budgets





Source: MIDAS IMS Health, MAT Q3 2014, Rx; Brazil and Mexico Non Retail Sales are included; Share of growth in LC$

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Biologics increasingly feature as key therapies

Payers see their costs

Global top 10 products 2009-14

	2009	2010	2011	2012	2013	2014
1	LIPITOR	LIPITOR	LIPITOR	SERETIDE	HUMIRA	HUMIRA
2	PLAVIX	PLAVIX	PLAVIX	CRESTOR	SERETIDE	LANTUS
3	NEXIUM	SERETIDE	SERETIDE	HUMIRA	CRESTOR	ABILIFY
4	SERETIDE	NEXIUM	NEXIUM	NEXIUM	ENBREL	SERETIDE
5	SEROQUEL	SEROQUEL	CRESTOR	LIPITOR	NEXIUM	ENBREL
6	ENBREL	CRESTOR	SEROQUEL	ENBREL	ABILIFY	CRESTOR
7	REMICADE	ENBREL	HUMIRA	REMICADE	REMICADE	REMICADE
8	ZYPREXA	REMICADE	ENBREL	PLAVIX	LANTUS	NEXIUM
9	CRESTOR	HUMIRA	REMICADE	ABILIFY	CYMBALTA	SOVALDI
10	SINGULAIR	ZYPREXA	ZYPREXA	LANTUS	MABTHERA	MABTHERA

Small molecule products Biologic products

Source: IMS Health, MIDAS, MAT Sep 2014

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In Germany we really see the importance of biologic therapies

Top 10 products 2009-14

	2009	2010	2011	2012	2013	2014
1	HUMIRA	HUMIRA	HUMIRA	HUMIRA	HUMIRA	HUMIRA
2	ENBREL	HERCEPTIN	HERCEPTIN	HERCEPTIN	AVASTIN	AVASTIN
3	SERETIDE	ENBREL	ENBREL	ENBREL	ENBREL	ENBREL
4	GLIVEC	AVASTIN	MABTHERA	MABTHERA	HERCEPTIN	HERCEPTIN
5	REBIF	MABTHERA	AVASTIN	AVASTIN	MABTHERA	MABTHERA
6	LOVENOX	SERETIDE	SEROQUEL	LOVENOX	LYRICA	XARELTO
7	SYMBICORT	SEROQUEL	GLIVEC	SPIRIVA	COPAXONE	LYRICA
8	HERCEPTIN	GLIVEC	LOVENOX	GLIVEC	REMICADE	ZYTIGA
9	SEROQUEL	REBIF	COPAXONE	LYRICA	AVONEX	REMICADE
10	SPIRIVA	LOVENOX	REBIF	LUCENTIS	REBIF	REBIF

Small molecule products Biologic products

Source: IMS Health, MIDAS, MAT Sep 2014

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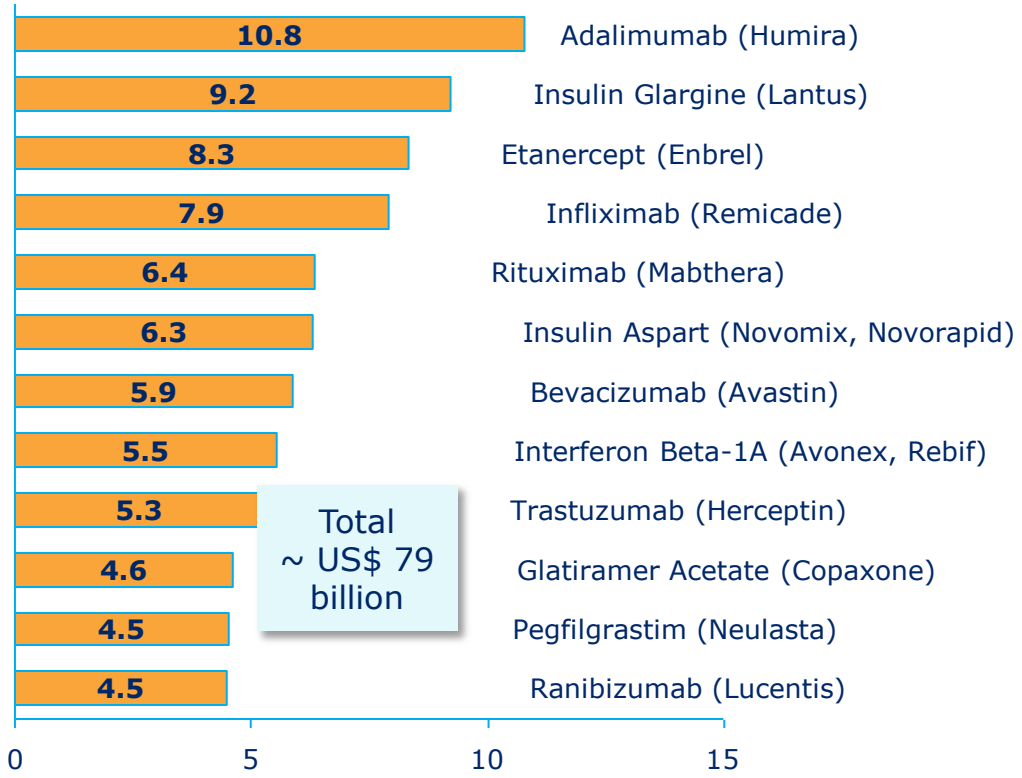
It's the loss of exclusivity that drives biosimilar interest

All these products will lose patent protection by 2020
(except Enbrel, US patent extended until 2028)

Global Sales (MAT 06/2014), US$ billion



EU expiry date	US expiry date
2018	2016
2015	2016
2015	*2028 (extended)*
2015	2018
Expired	2018
Expired	Expired
2019	2019
2015	2016
Expired	2019
2017	2015
2015	2015
2016	2016

Not considered existing biosimilars such as Epoetin Alfa expired in EU, but still patent protected in the US

Source: IMS MIDAS, 06/2014, Rx bound, IMS Patent focus

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In contrast to small molecule GX, biosimilar development and marketing pose serious challenges for aspiring players

Biosimilars vs. Generics – *a different game?*

CLINICAL DEVELOPMENT

Average cost is around 200M$**, with a significant range of variation (from 40 to 375 M$) **vs. 1 to 4M$ for a generic drug

REGULATORY AND MARKET ACCESS

Uncertain regulatory framework (aside from Europe), price competition less relevant compared to generics

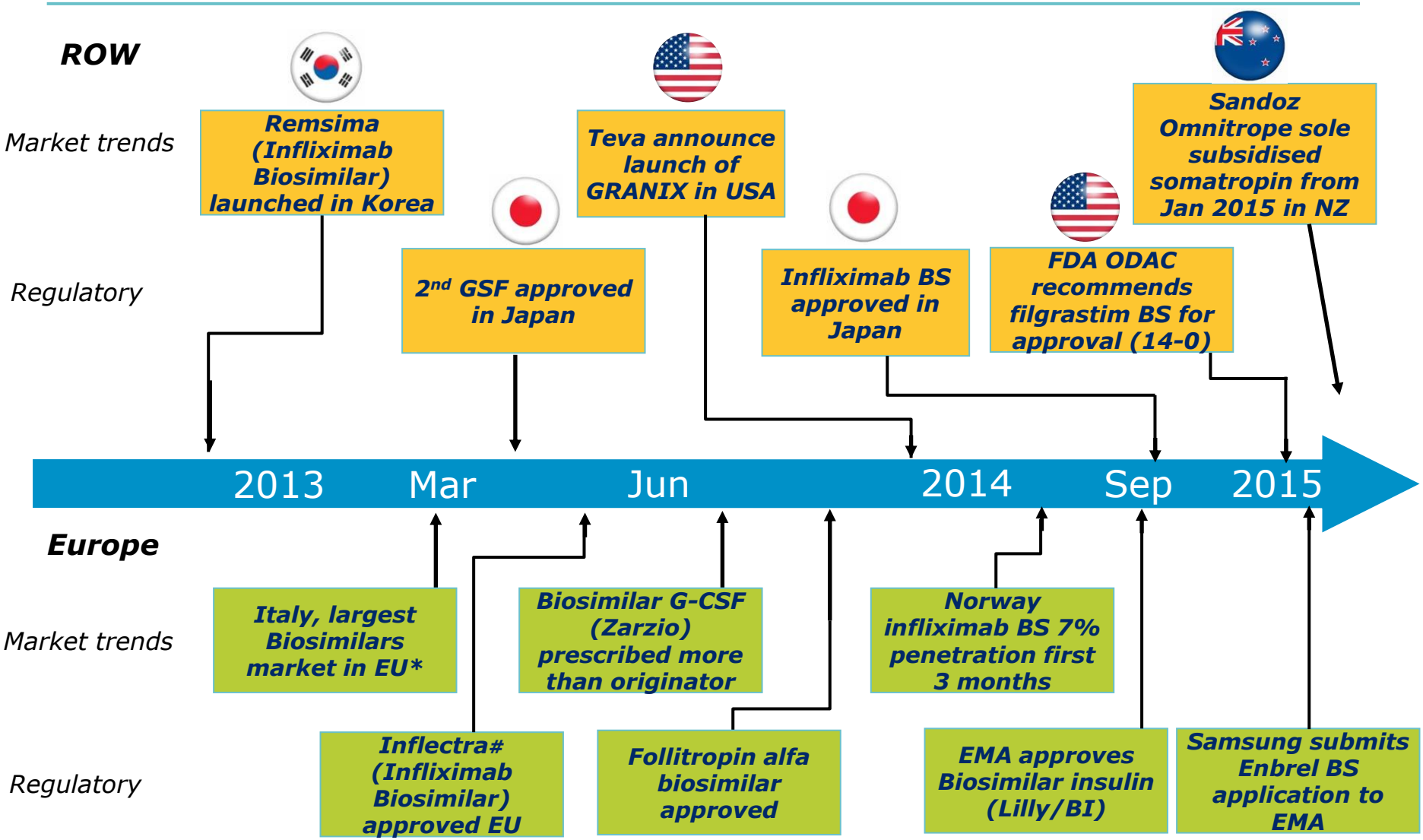
MANUFACTURING COSTS

Difficulties in rationalizing manufacturing costs due to limited scale, at least in the short term

SALES AND MARKETING CAPABILITIES

Need to adopt a branded mentality to win stakeholder trust

Biosimilars are making steady progress...



Source: Secondary research. List not exhaustive. (*) at ex-manufacturer price levels, not including rebates and discounts.
(#) Recommended for RA (Rheumatoid arthritis), CD (Crohn's disease), UC (Ulcerative colitis), AS (Ankylosing spondylitis), PA (Psoriasis), PsA (Psoriatic arthritis)

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Learning from the biosimilar experience

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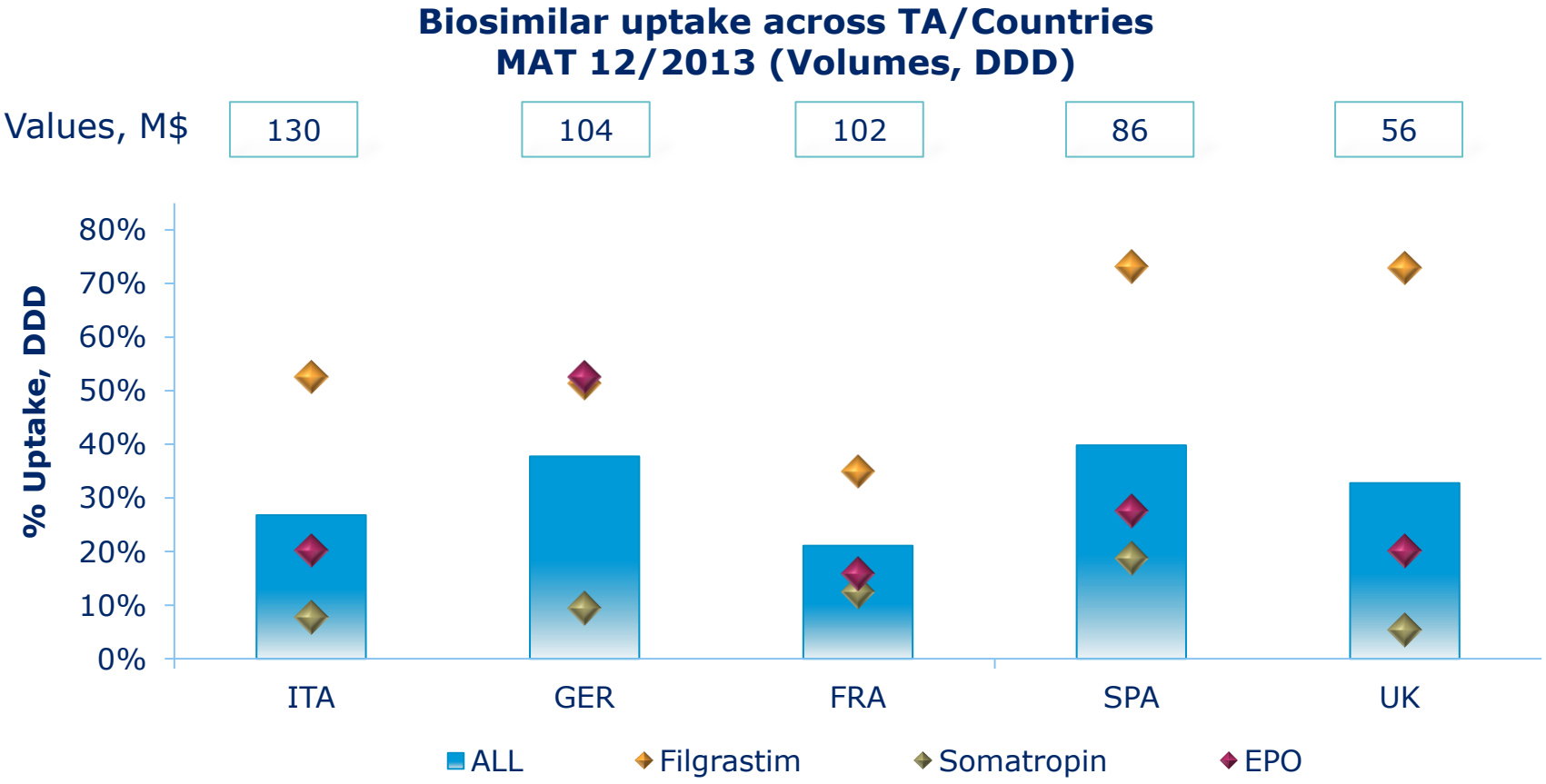
What has been the uptake of biosimilars in Europe?

Experience with biosimilars illustrate variations at the therapy area, country and molecule level



Source: IMS MIDAS, MAT 12/2013. Uptake is defined as penetration of accessible market. This includes reference and non reference prods

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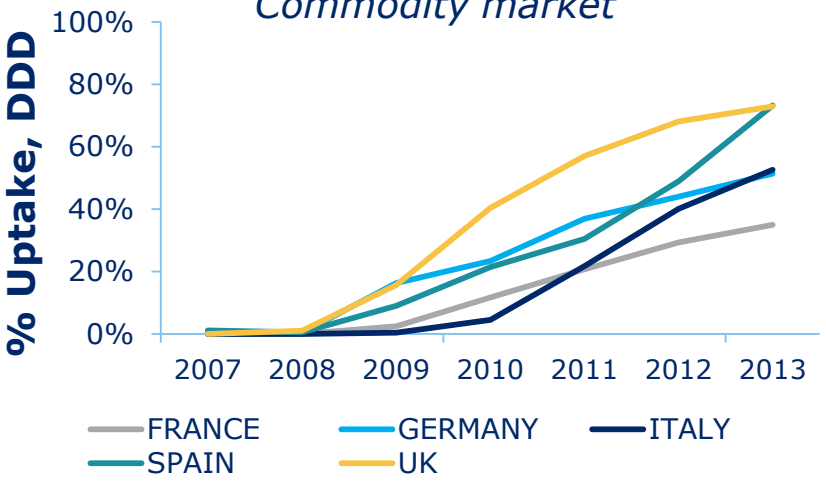
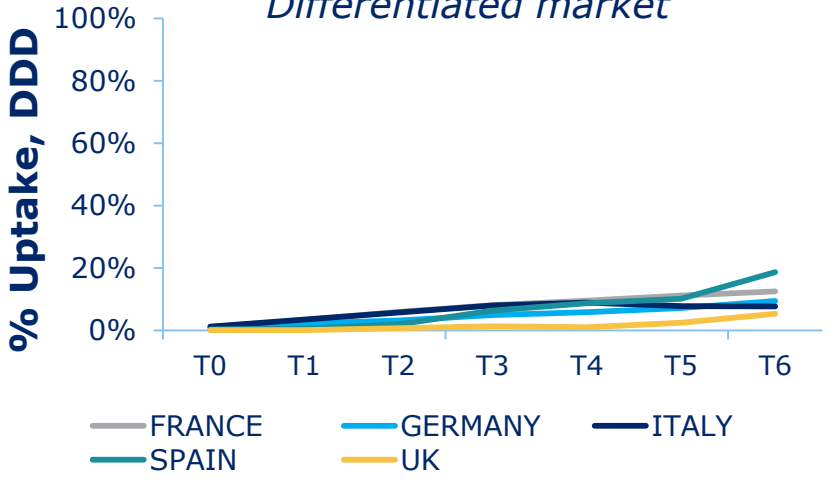
Penetration of biosimilars across different therapy areas has been variable for a number of reasons

Stakeholder landscape – payer-driven vs. multiple influencers – and treatment cycle are the key determinants

Filgrastim uptake 2007-2013, yearly
Commodity market



Somatropin uptake 2007-2013, yearly
Differentiated market



- ✓ Payer-driven market access (e.g. Tender, step-wise algorithms)
- ✓ Price-driven competition
- ✓ Acute treatment and/or frequent cycling among therapies

- ✓ Complex stakeholder landscape with higher physician influence
- ✓ Competition based on multiple marketing levers
- ✓ Chronic treatment and/or long therapeutic cycles

Source: IMS MIDAS year 2013. (*) Uptake is defined as penetration of accessible market. This includes reference and non reference prods

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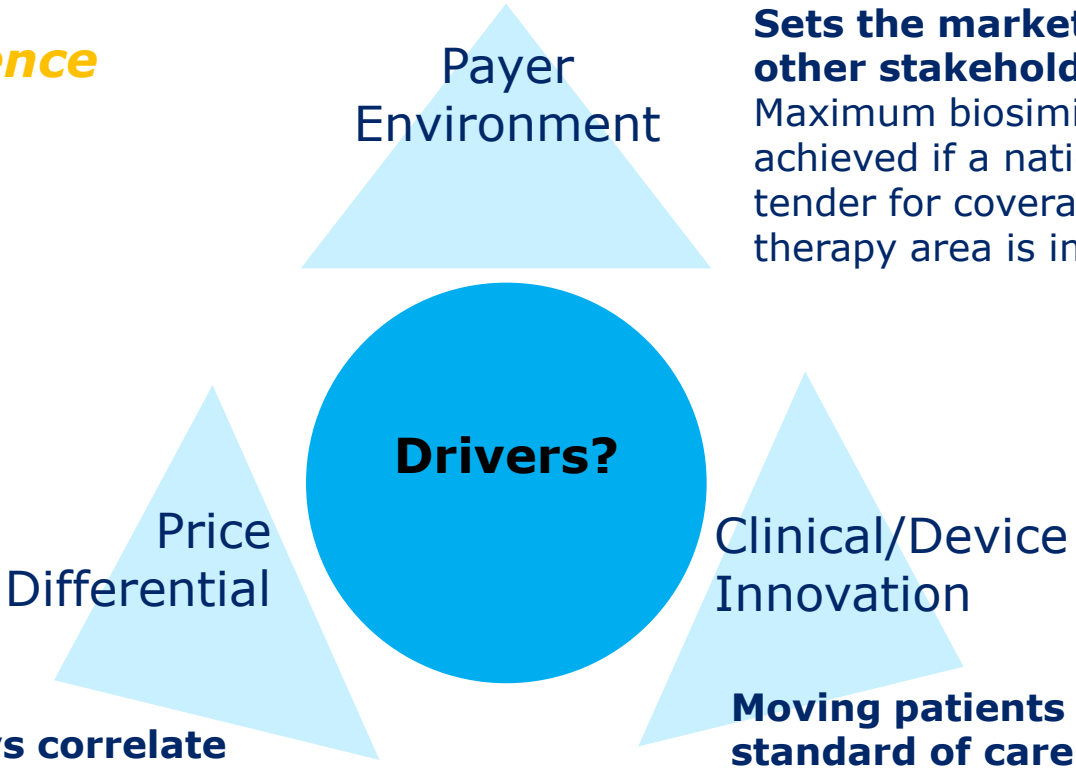
What really drives Biosimilars uptake?

Best evidence learnings



Sets the market environment for other stakeholders
Maximum biosimilar uptake could be achieved if a national single sourced tender for coverage of the entire therapy area is implemented

Doesn't always correlate to biosimilar uptake
Actions taken by manufacturers in specific markets are observed as having an impact on biosimilar uptake and affecting the competitive environment

Moving patients to the next standard of care
Second generation products have in some cases had significant impact:
- Sometimes by strategic pricing
- Sometimes by recognized value or improved outcomes

Source : IMS Health insight

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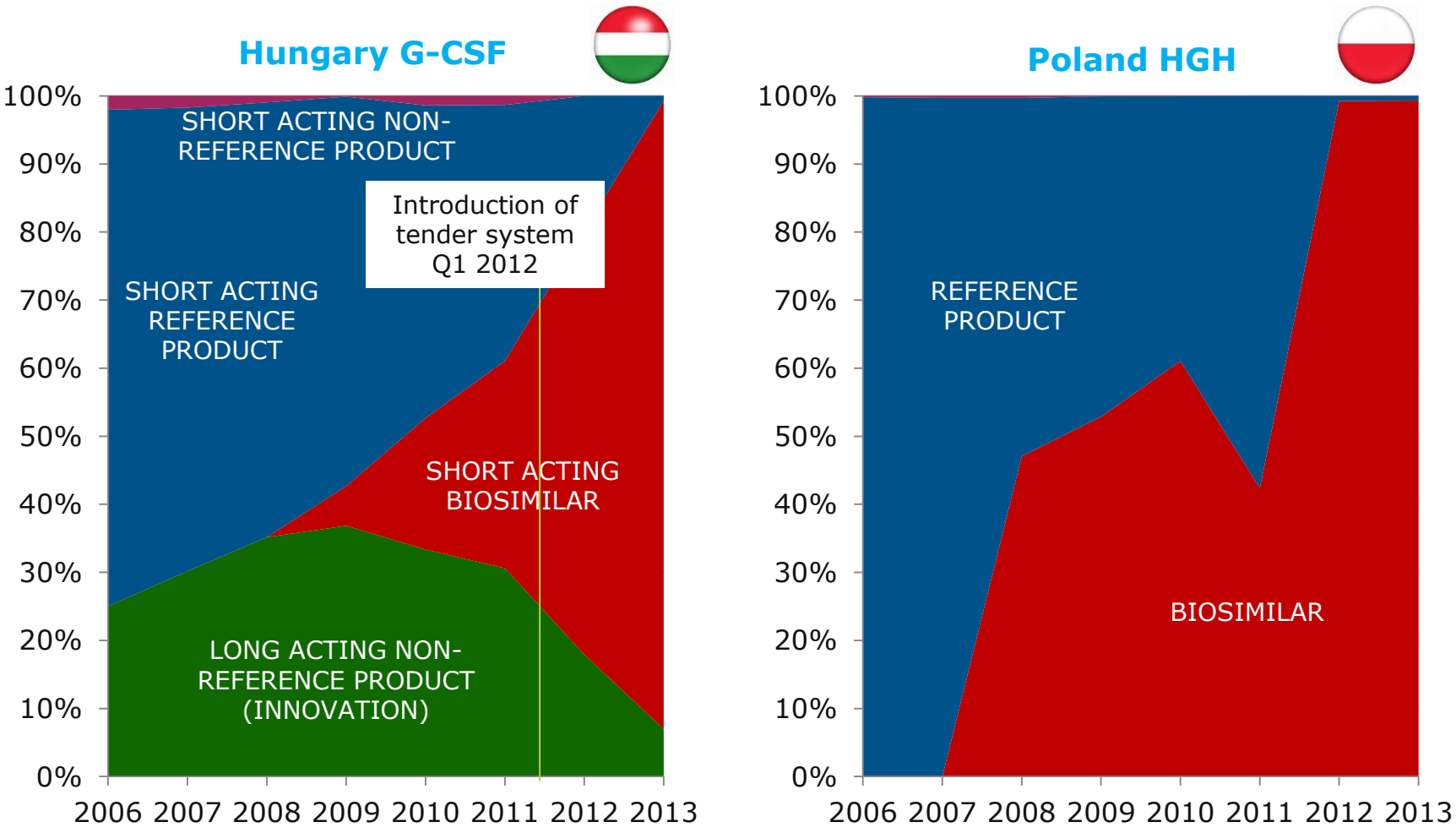
Under tender/blind-bidding procurement systems, market evolution may play differently



Source : IMS Health MIDAS 2013

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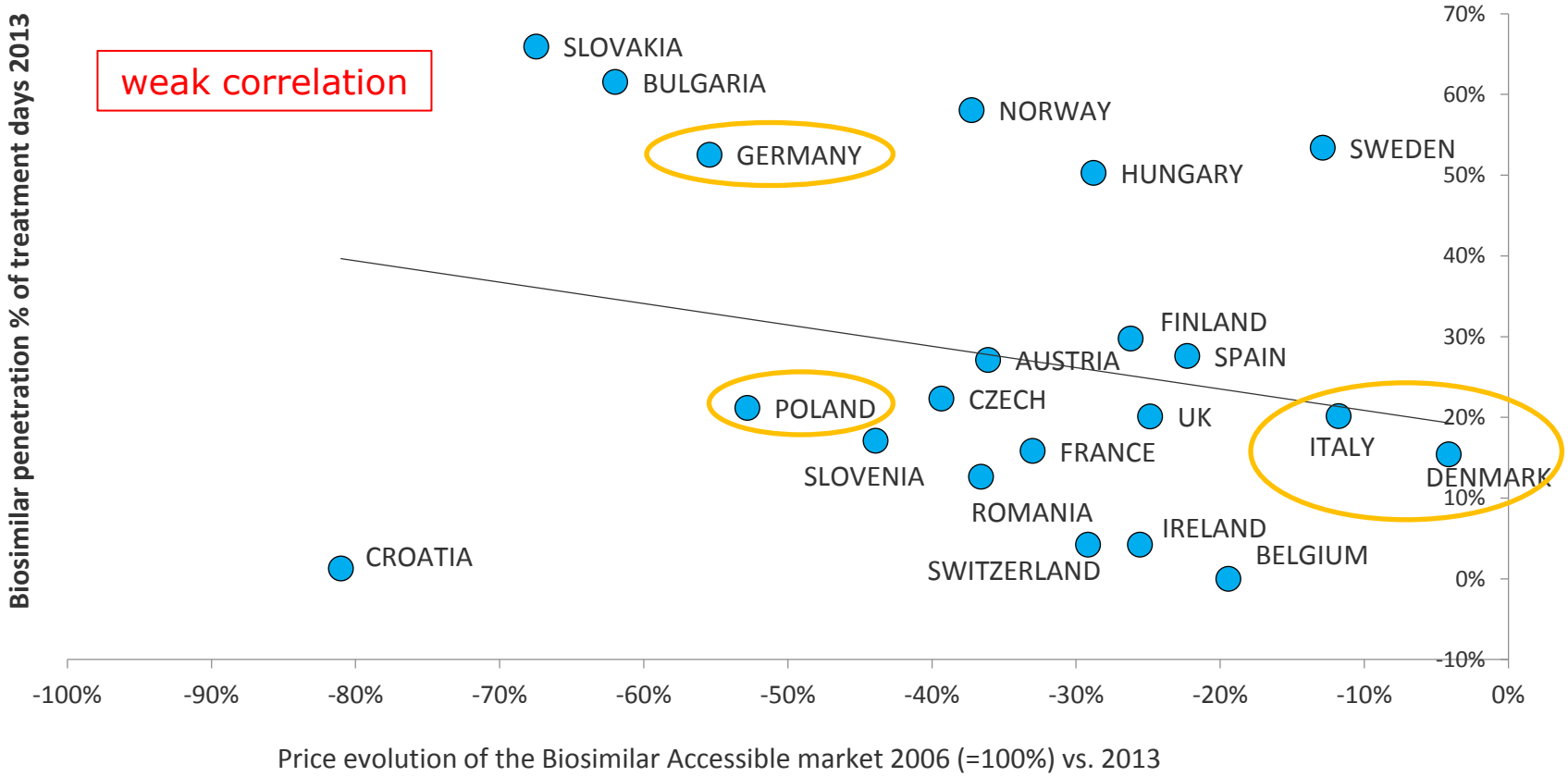
Does accessible market price reduction correlate to biosimilar uptake?

EPO: 2013 uptake of Biosimilars vs. 2006-2013 price evolution of the accessible market



Source : IMS Health MIDAS 2013

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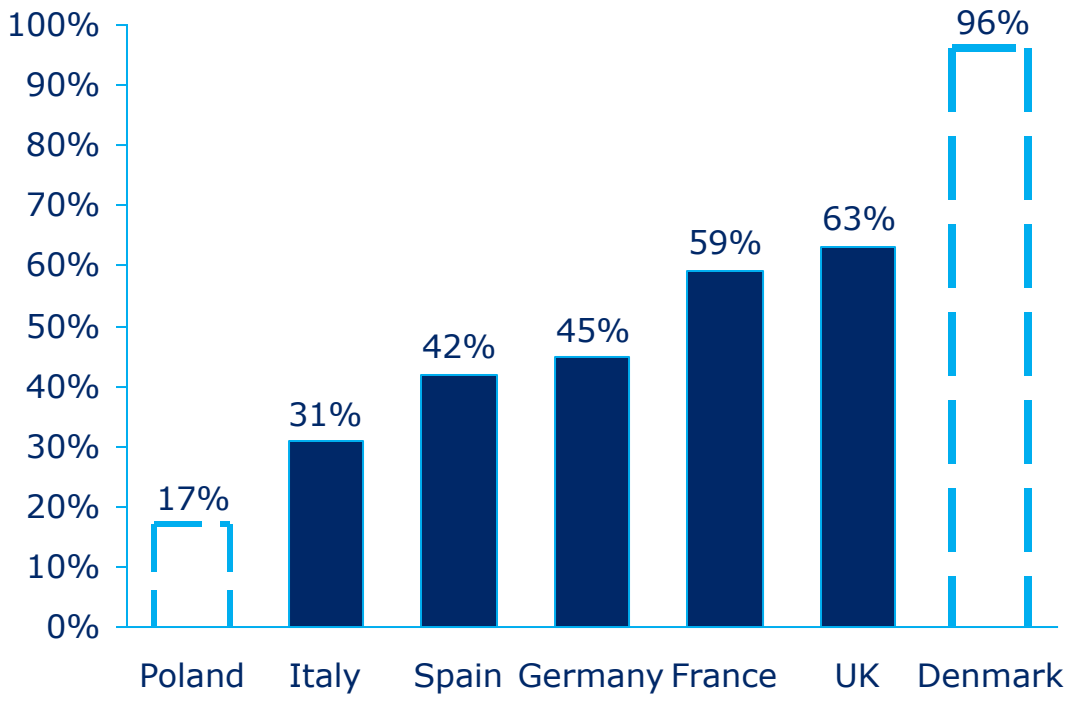
To what extent has usage shifted to 2nd generation products?

EPO: uptake of 2nd generation in the total market (% of treatment days 2013)



Comments

For EPO's, patent protected 2nd generation products are available.

- Denmark has low uptake of EPO biosimilars as the market shifted to 2nd generation
  → successful originator strategy

- Differently in Italy and Poland, market remained on first generation EPO
  → Originators are successfully competing with pricing strategy despite significant biosimilar price differential (Poland)

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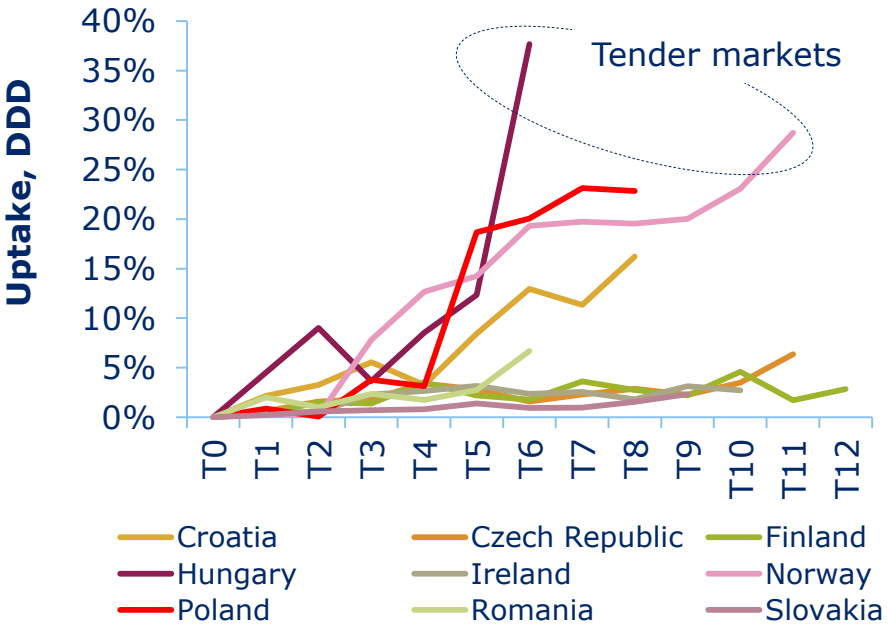
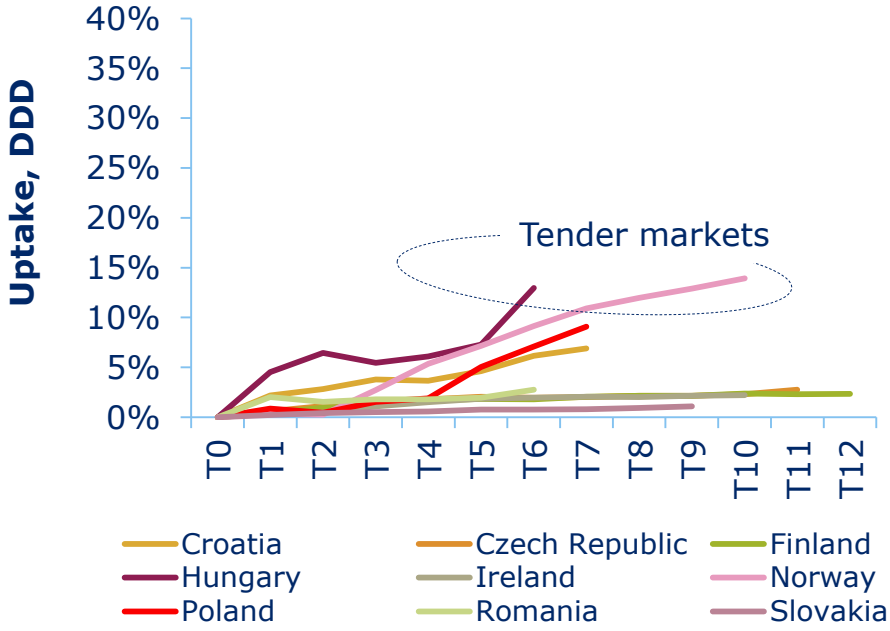
Infliximab biosimilar has shown strong uptake in tender markets but much more moderated in others

Will patterns of use and different mode of action influence the market?

Infliximab Monthly uptake
Normalised uptake



Infliximab Monthly uptake
*Cumulative uptake**



Will Infliximab BS be used instead of the originator? Will it impact the usage of other anti-TNFs such as Humira and Enbrel? Will MABs be used more widely?

*Source: IMS MIDAS monthly Oct 2014. Penetration calculated in treatment days (TD). *still normalised by launch date*

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Learnings so far...

- Biosimilar uptake is highly diverse across markets and between therapy areas
- There is a weak correlation between biosimilar uptake and the price differential between biosimilar and originator
- The payer framework establishes the decision drivers allowing for biosimilar uptake, although innovation strategies sometimes work
- The next wave of Biosimilars is going to be different and the past is not necessary a good indicator of what will happen
- Understanding and balancing payers' needs will be necessary to drive biosimilars uptake or attempting to protect brands

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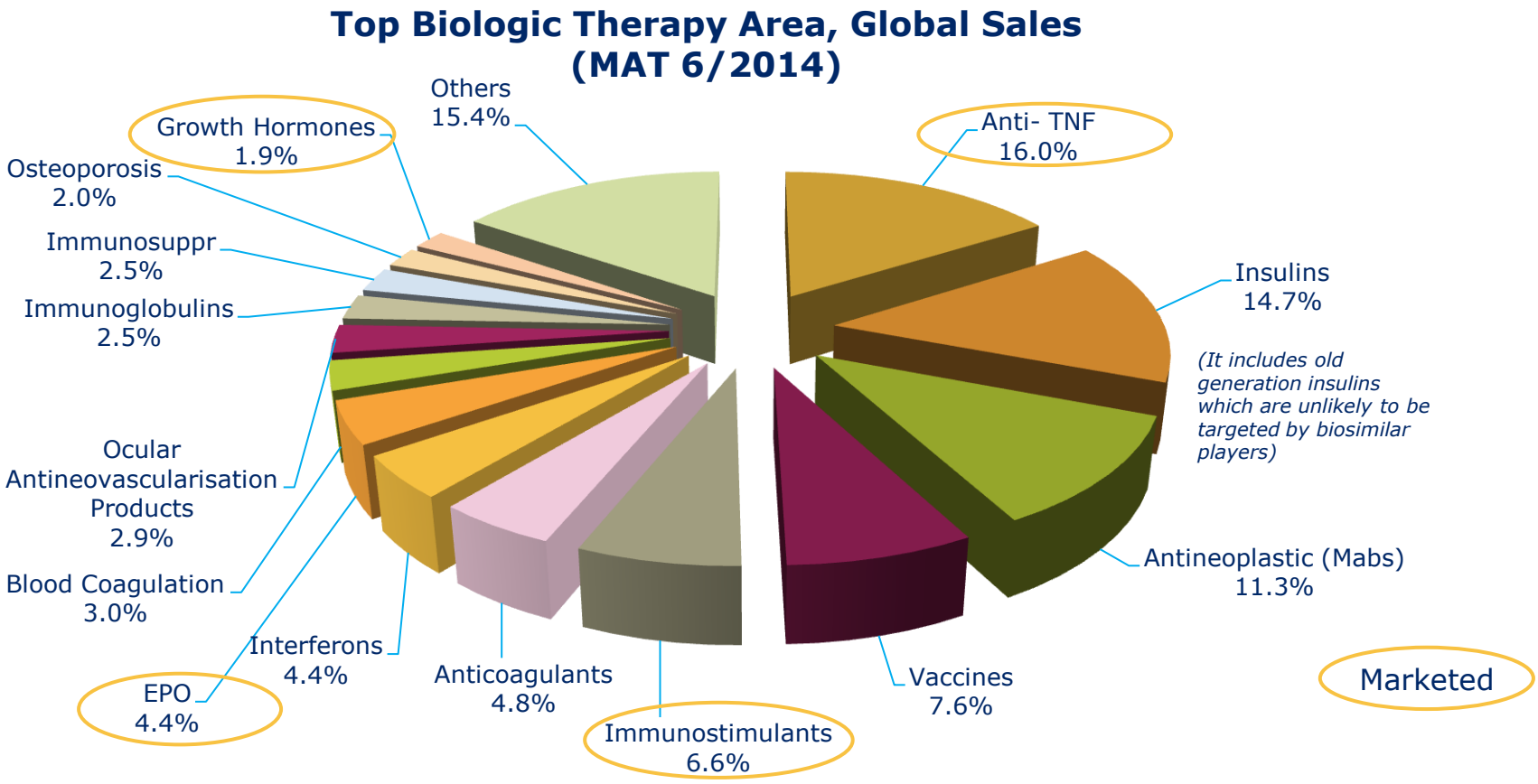
Anti-TNF, insulins and onco MABs are the key biologics



Source: IMS MIDAS, Q2 2014; Rx

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The most popular biosimilar targets are MABs

The most popular biosimilar targets under development

Originator brand-name	Active substance	Originator company	Therapeutic area	2013 sales (US$ billion)	No. of biosimilars in development	Biosimilar front runner
Avastin	bevacizumab	Roche	Bowel/breast/colon cancer	7.0	15	Amgen
Enbrel	Etanercept	Amgen/Pfizer	Arthritis Psoriasis	8.3	27	Sandoz/Samsung Bioepsis
Herceptin	Trastuzumab	Roche	Breast/stomach cancer	6.8	21	Amgen
Humira	Adalimumab	AbbVie	Arthritis Ulcerative colitis Crohn's disease Ankylosing spondylitis	10.7	13	Amgen
Rituxan	Rituximab	Roche	Arthitis Non-Hodgkin lymphoma (NHL) Leukaemia	8.6	35	Boehringer Ingelheim
Total				**49.8**	**125**	

Source: GABI

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Barriers to effective biosimilar penetration vary but will be higher for Mabs than recombinants

Barrier

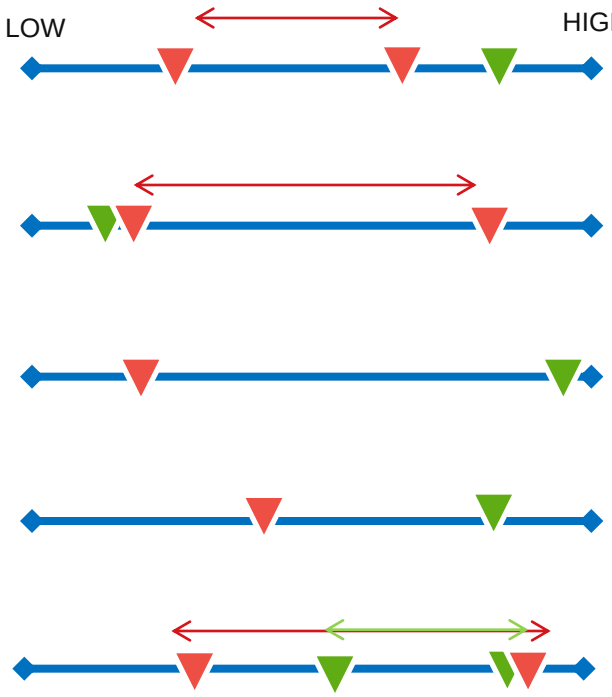
New to repeat Rx opportunities
(high =attractive to biosimilars)

Indication extrapolation
(high =attractive to biosimilars)

Efficacy/safety acceptance
(High=attractive to biosimilars)

Market acceptance of biosimilars
(High=attractive to biosimilars)

Number of innovative competitors
(Low=attractive to biosimilars)



▼ Mab ▼ Recombinant protein

Implications

- Oncology Mabs will have higher new patient opportunities than autoimmune
- Significant indication extrapolation for many oncology products and autoimmune
- Very high level of efficacy and safety scrutiny for Mabs
- Market creation will mean higher investment and harder for Mabs than recombinants

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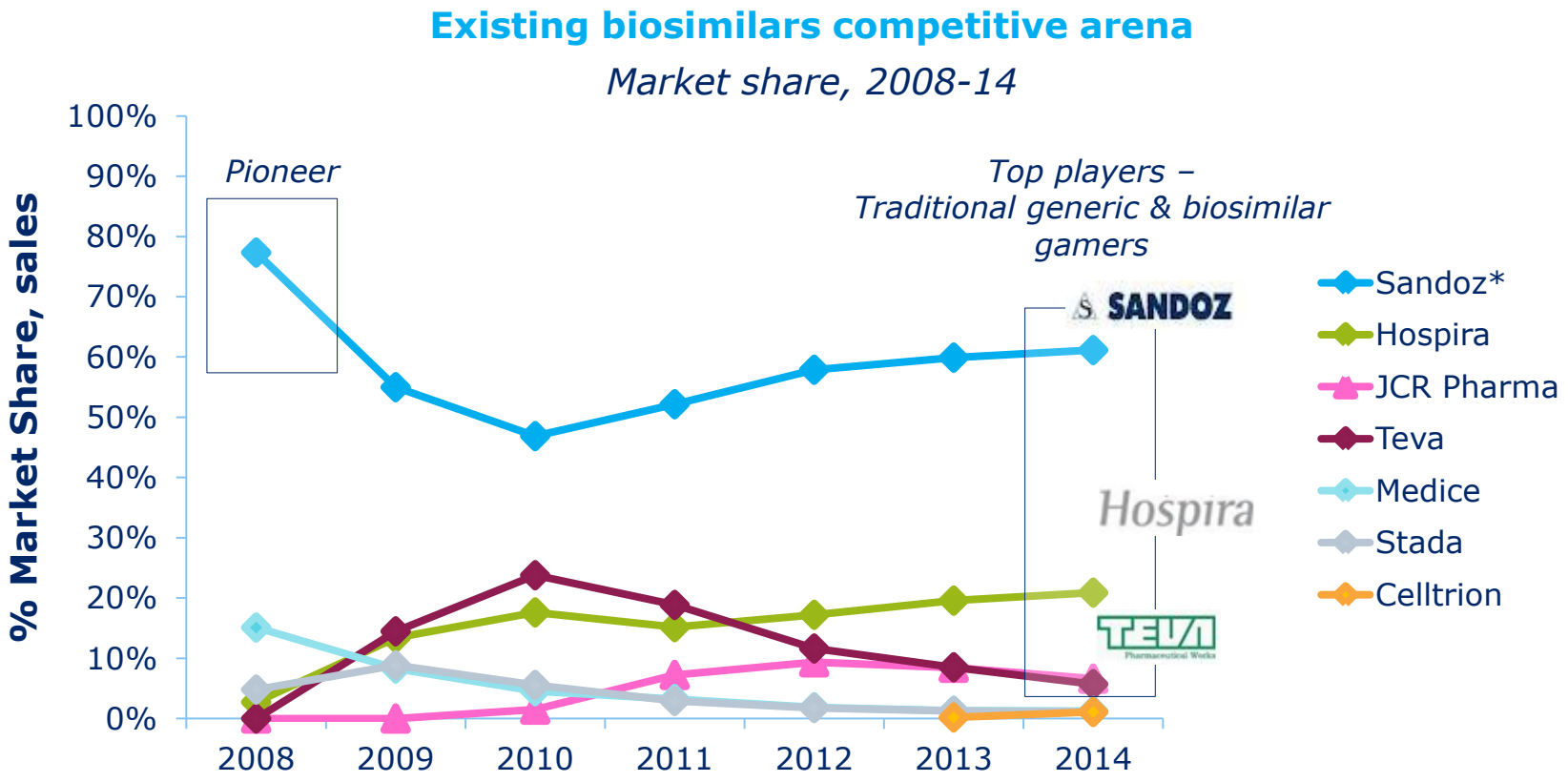
The top players are major generic companies such as Teva, Sandoz along with specialists Hospira



(*) it includes bio-comparables abbreviated approval of Omnitrope in North America

Source: IMS MIDAS MAT Sep 2014

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But many other companies have recently confirmed and expanded biosimilar development programmes

Nov 2014, Gabi.net

– ***Amgen*** *expands biosimilar programme. In addition to the existing six biosimilar programmes , Amgen has also initiated three additional biosimilar programmes, bringing its* ***total biosimilar programmes to nine.***

AMGEN

Sep 2013– ***Baxter and Coherus*** *to collaborate on biosimilars*

Baxter Coherus BIOSCIENCES

Sep 2014 – ***Merck KGAA plans to step up investments in biosimilars during 2015****. The company plans to invest an additional US$130–150 million in biosimilars for 2015 (on top of €100 million for 2014)*

MERCK

...who's next?

Apr 2014 –
Boehringer ingelheim *annual conference. Chairman Andreas Barner confirmed that all these compounds are in advanced stages of development. "We see* ***biosimilars*** *as a future* ***growth field****"*

Boehringer Ingelheim

Feb 2014 – ***Merck and Samsung Bioepis have expanded their collaboration*** *with an agreement to develop, manufacture and commercialize MK-1293 (biosimilar glargine)*

SAMSUNG MERCK

Source: Web research. IMS Health. List not exhaustive

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4 categories of players will mean very different go-to market strategies, pricing and competitive behaviour

Is there going to be space for everyone?

Innovator companies	Generics companies	Other players
MERCK SERONO, MERCK, Pfizer, Daiichi-Sankyo, Boehringer Ingelheim, biogen idec, Baxter, AMGEN, Lilly	SANDOZ, Hospira, TEVA Pharmaceutical Works, Mylan, STADA Arzneimittel, actavis creating value in pharmaceuticals, DR. REDDY'S, Cipla Caring for life, GEDEON RICHTER	FUJIFILM (Fujifilm Kyowa Kirin Biologics), SAMSUNG, GE Healthcare

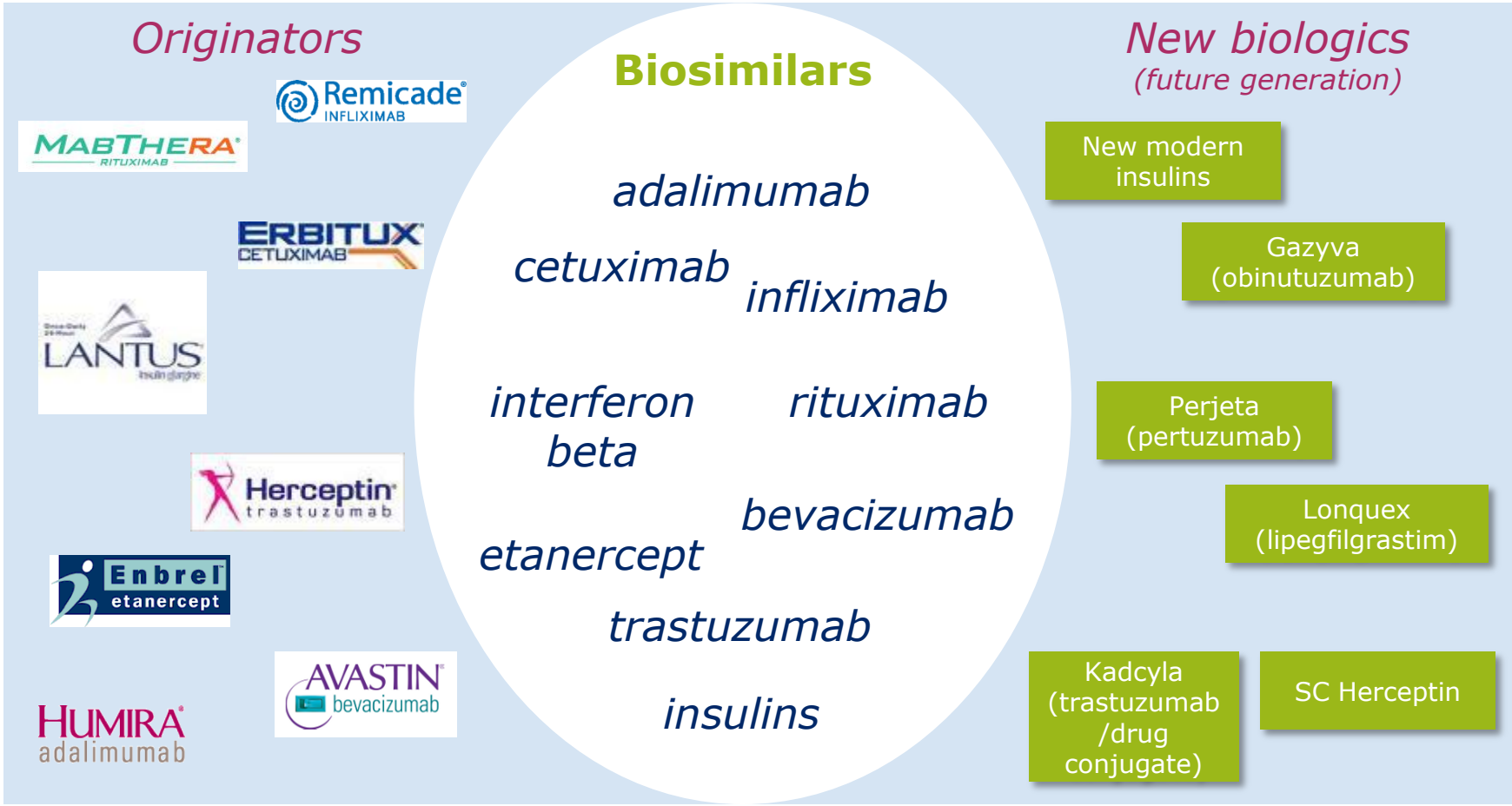
CRAMS* providers / Emerging market domestic players

Biocon, Lonza, INTAS Expressions for healthy life, Zydus dedicated to life, QUINTILES, Harvest Moon PHARMACEUTICALS USA. INC, CELLTRION, IBA BIOTON, PAREXEL, WOCKHARDT

*CRAMS, Contract Research and Manufacturing Services ** Based on press release news

Success and speed of biosimilar uptake will also be dependent on the strategy employed by originators

Many R&D companies have launched or will launch next generation biologics



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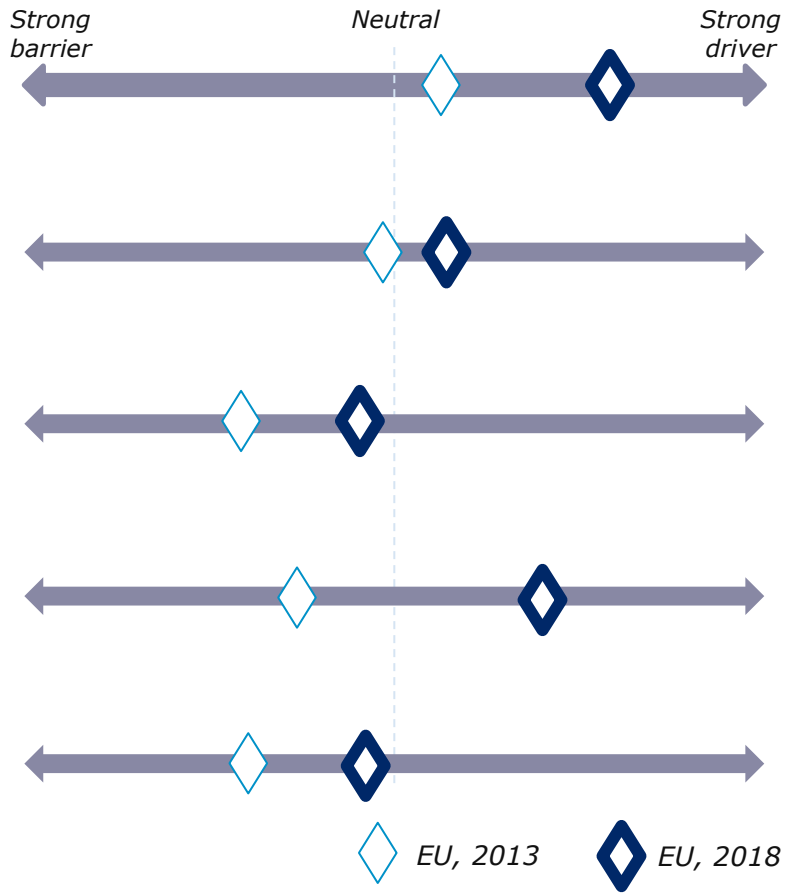
Payers and policy-makers are rising as biosimilar advocates

Superior clinical results with biologics will gain clinician and patient attention whilst associated costs will prove problematic for payers

Stakeholder drivers

Payer / Government	• Healthcare rationalization • Ensure safety and clinical efficacy • Leverage macroeconomic growth through biosimilars
Physician	• Safety and clinical efficacy concerns • Need to build learning curve on biosimilars • Reaction to differ by therapy area
Patient	• Looking for broader and affordable access • Likely to be influenced by physician advice
Aspiring player	• Massive capitals invested on biosimilars • Branded players bringing in R&D capabilities • Growing specialization along the value chain (CRAMS providers)
Originator	• Lifecycle management • Patent disputes • Active players in the biosimilar arena

Impact on biosimilars market



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Conclusions

- Biopharmaceuticals represent many of the future new clinical advances
- Superior clinical results will gain clinician and patient attention whilst associated costs will prove problematic for payers
- Payers are looking for cost savings but also low risks
- The first wave of mAb biosimilars has come from a new market player with a different go-to market strategy, competitive behaviour and expectations
- Many companies are competing to enter, with potentially just one lever to use: PRICE
- Plan for the unexpected!

Thank you!

- For further information please contact:
  - Doug Long dlong@us.imshealth.com