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Biosimilar Adoption & Barriers to Success: Current & Future Considerations

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Our Presenter

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Speaker Disclosure

- The presenter has no real or perceived conflicts of interest related to this presentation
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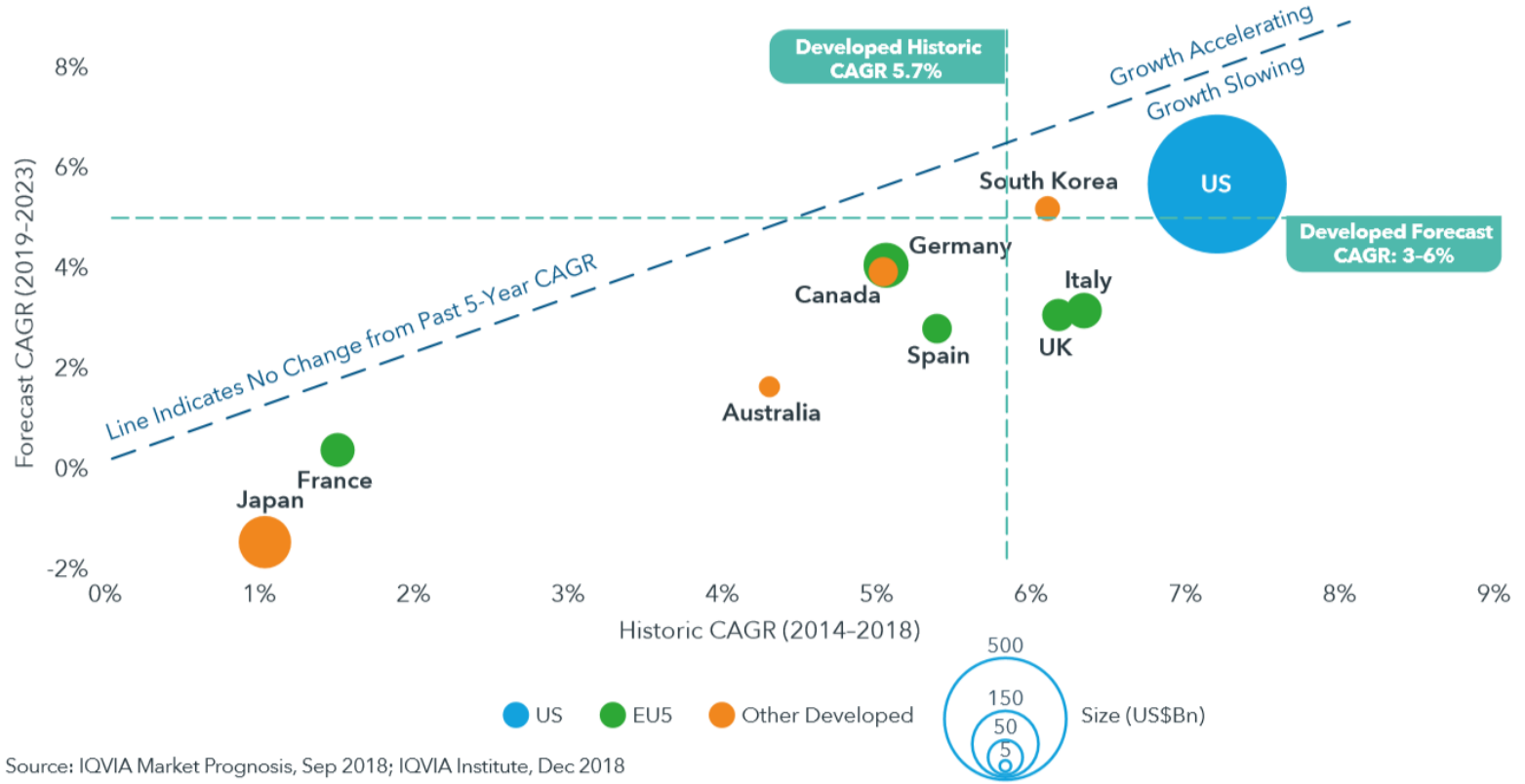
Learning Objectives

At the end of this session, participants should be able to:

1. Review current and future economics of biologics
2. Discuss challenges with biosimilar adoption within health systems
3. Describe the role of data and education in helping to improve biosimilar adoption with high-touch patient support

Global Medication Spending Growth by Region

Developed Markets Historic and Forecast Spending Growth by Country



Source: IQVIA Market Prognosis, Sep 2018; IQVIA Institute, Dec 2018

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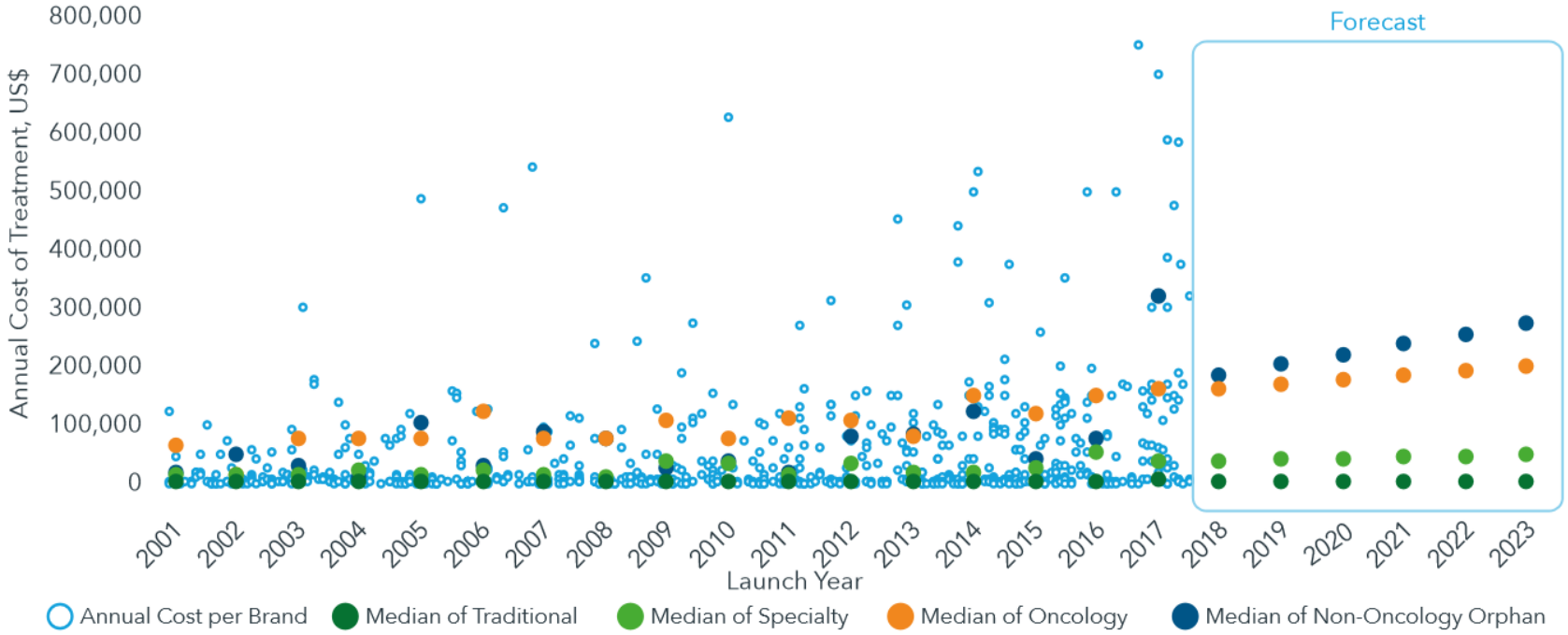
Annual U.S. Drug Pricing Trends & Forecast into 2023

Annual & Median Costs of U.S. Brands by Type & Launch Year U.S.$



Source: IQVIA National Sales Perspectives, Dec 2017; IQVIA Institute, Dec 2018
Notes: Annual costs based on invoice prices, with overall invoice-level spending divided by estimated numbers of patients. Patient estimates are based on audited volumes assuming all patients use the drug according to the approved label. Products are included in medians based on segment assignments. Oncology includes both orphan and non-orphan products. All other products that have orphan indications are grouped together and some products have both orphan and non-orphan indications in this group. Specialty and traditional products exclude orphan or oncology products but are otherwise defined according to IQVIA definitions. Projected median costs are based on simple extrapolation of the medians in the prior ten years.

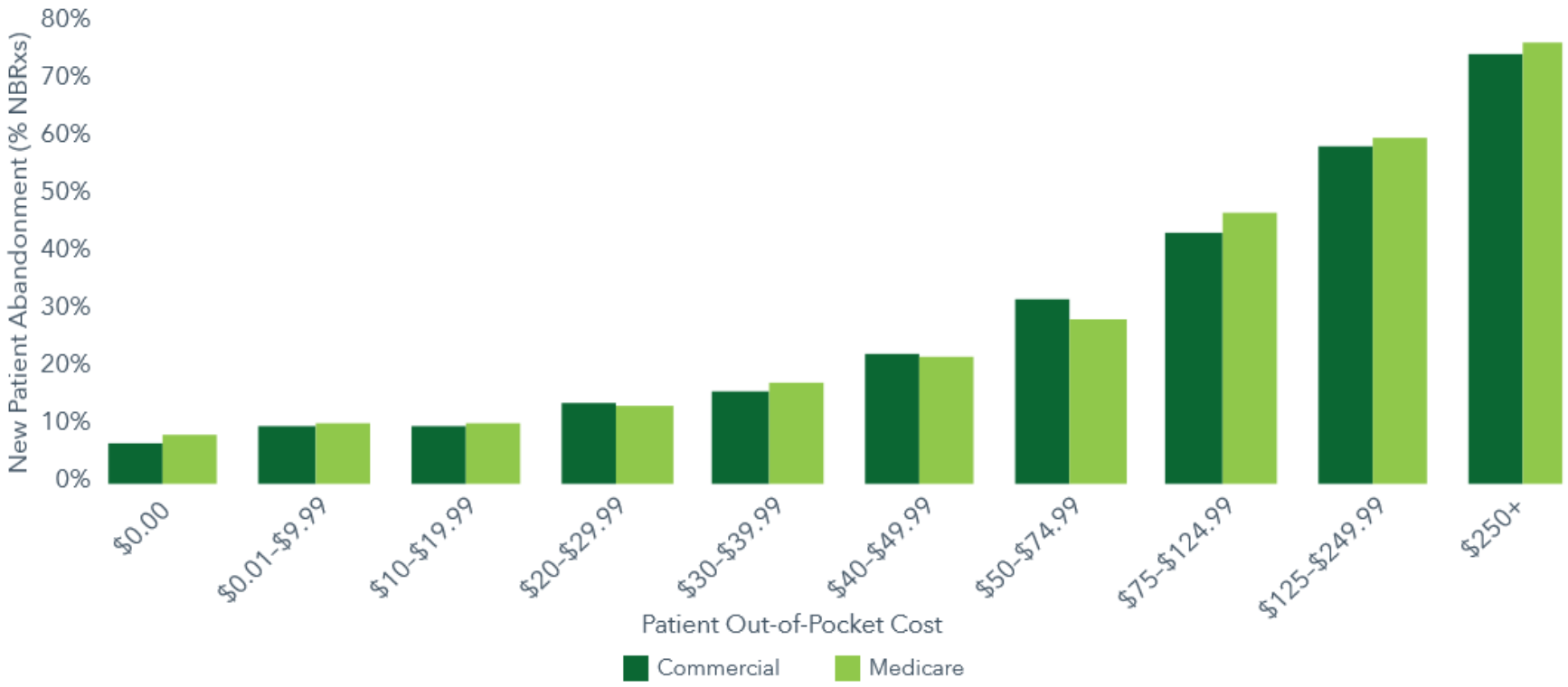
ICER Unsupported Price Increase Report, 2019 Assessment

Rank	Drug	Q42016 to Q42018 Percentage Change		Increase in Drug Spending Due to Net Price Change ($M)
		WAC	Net Price	
1	Humira (Adalimumab)	19.1%	15.9%	$1,857
2	Rituxan (Rituximab)	17.0%	23.6%	$806
3	Lyrica (Pregabalin)	28.3%	22.2%	$688
4	Genvoya (EVG/COBI/FTC/TAF)	14.3%	21.7%	$651
5	Truvada (TDF/FTC)	14.3%	23.1%	$550
6	Neulasta (Pegfilgrastim)	14.6%	13.4%	$489
7	Cialis (Tadalafil)	26.2%	32.5%	$403
8	Tecfidera (Dimethyl Fumarate)	16.7%	9.8%	$313
--	Revlimid (Lenalidomide)	25.8%	--	--

Script Abandonment on the Rise

The rate of prescription abandonment increases as cost exposure to biologics rise

Exhibit 22: 30-Day New-to-Brand Abandonment by Patient Out-of-Pocket Cost in 2018 (Top Brands)



Source: IQVIA Formulary Impact Analyzer; IQVIA Analysis, Dec 2018

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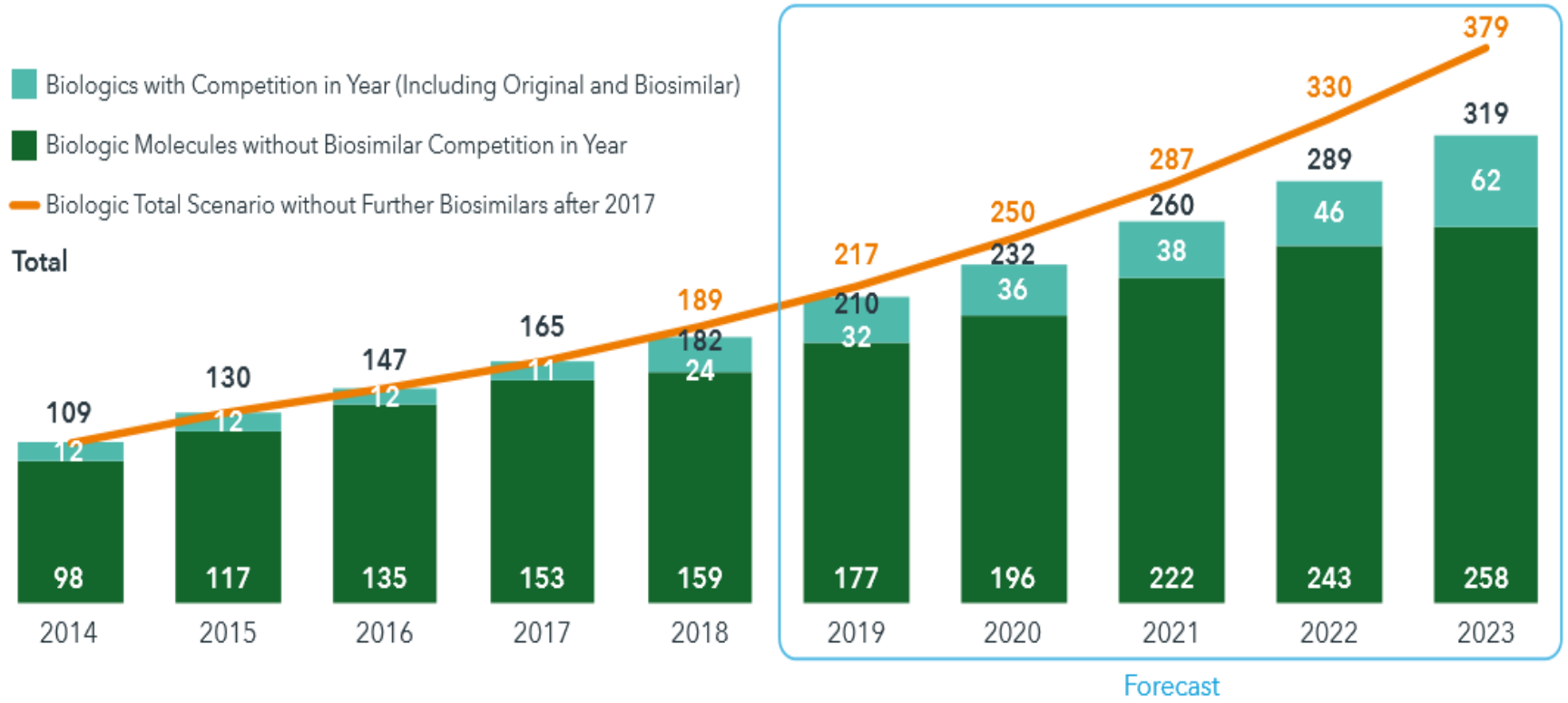
U.S. Biologic Spending

Spending by Competitive Status & Scenario w/o Future Biosimilar Molecules (U.S. Bn$)



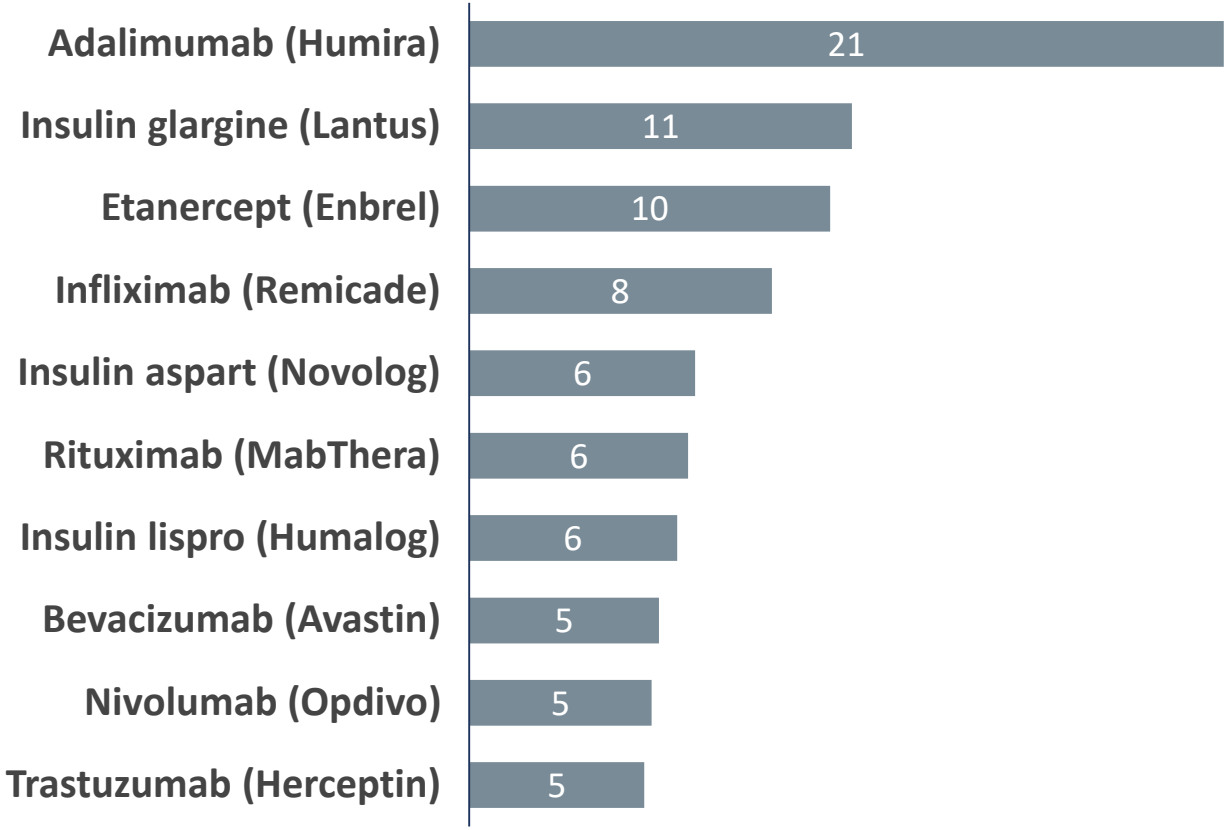
Source: IQVIA MIDAS, Jun 2018; IQVIA Institute, Dec 2018

Notes: Line on chart represents biologic spending using average growth of molecules not facing competition in 2017 continued to 2023 to represent what spending would have been without new molecules facing biosimilar competitors. Segments for biologics with and without competition are modeled using the average historic growth rates and expected entrance of biosimilars and price and volume changes associated with biosimilar entry.

Global Sales of Top 10 Biologics – Approximately U.S. $83 billion in 2017

HEADLINE

- The RAND Corporation estimates that biosimilar products can save the U.S. health system approximately $54 billion dollars over the next decade[1]



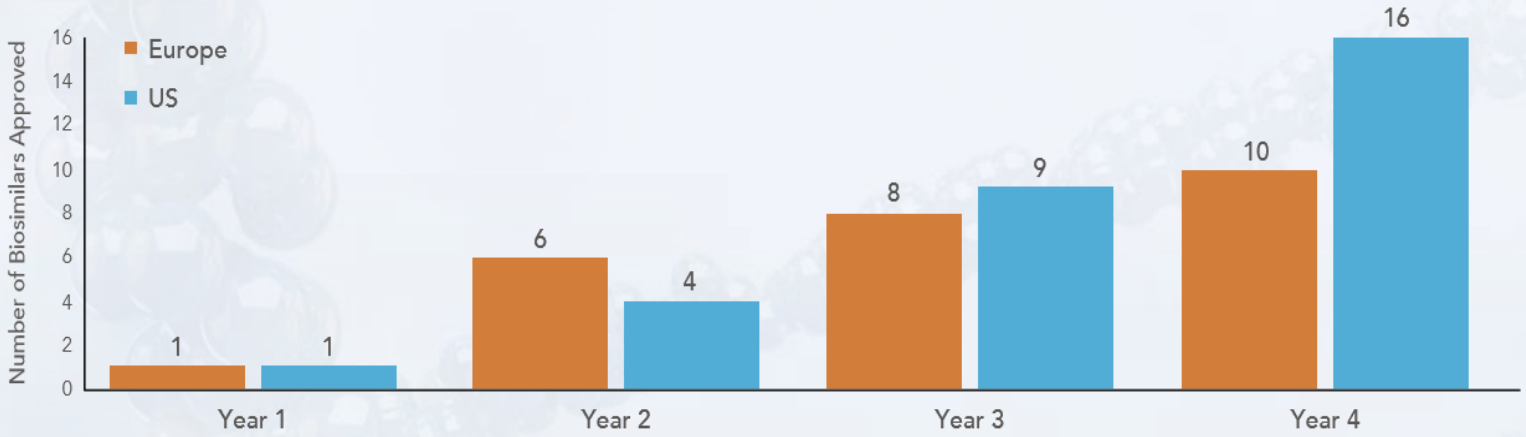
Source: IQVIA MIDAS, MAT June 2018; ARK Patent Intelligence, IQVIA Institute, Dec. 2018

Comparison of Biosimilar Markets in Europe & the U.S.

Europe has an advanced biosimilar market, with more approved products than the US (53 vs 17).[22,23] However, it should be noted that the 53 approved biosimilars in Europe are not distinct compounds. Some of the approved biosimilars are different brand names marketed under duplicate marketing authorizations or the same application. When the 2 markets are compared, starting from the point when they approved their first biosimilar, the US shows a higher rate of approvals. As **Figure 1** shows, by the end of Year 4, Europe had 10 biosimilars approved and the US had 16.[22,23]

Figure 1. Comparison of Europe and US Biosimilar Markets[22,23]

Cumulative Number of Biosimilars Approved for Marketing in Europe vs the US, Beginning With Year the First Biosimilar Was Approved



Source: https://www.amgenbiosimilars.com/pdfs/2019%20Trends%20in%20Biosimilars%20Report%20Electronic%20Version%20-%20USA-BIO-80182.pdf

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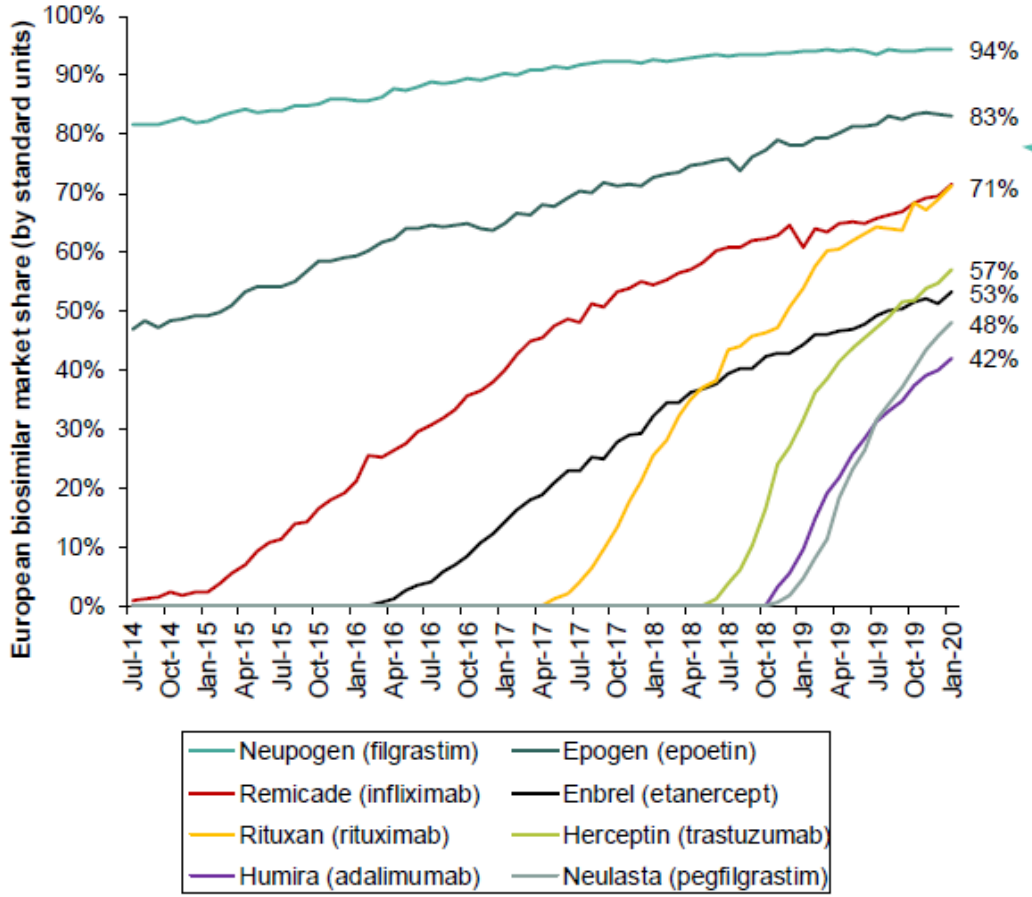
European Market Overview

Biosimilars as volume share of the reference molecule market



Oncology still going strong, Rituxan overtaking Remicade, Herceptin overtaking Enbrel, Neulasta distancing from Humira. Are incentives and market structures in oncology more favorable than immunology?

Roche commented on 4Q19 call that "…the bulk of the Herceptin losses and biosimilars happened in in 2019"

Source: IQVIA; Bernstein analysis

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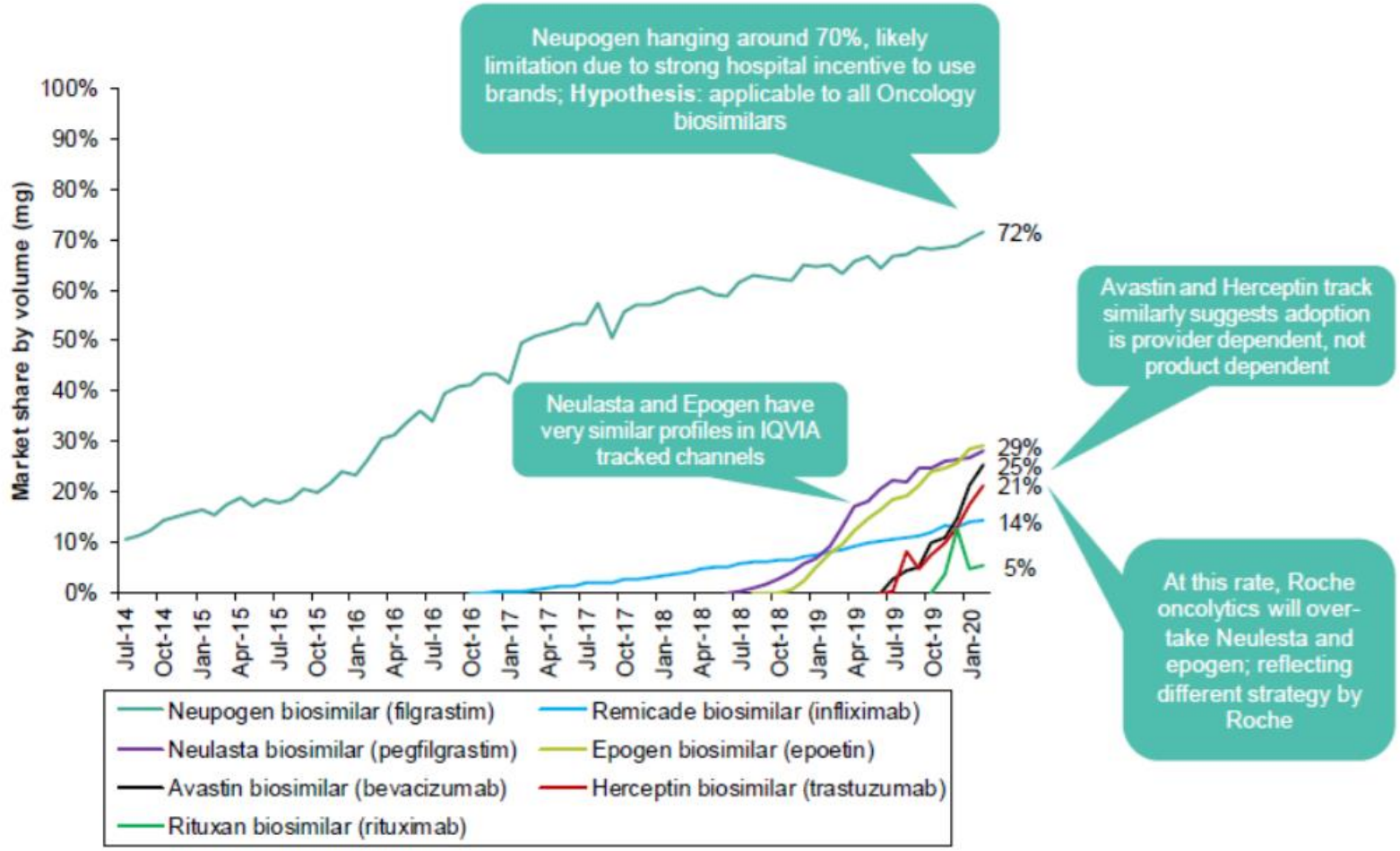
U.S. Market Overview: Biosimilar Volume Share of Reference Market



Source: IQVIA; Bernstein analysis
Note: Epogen market is defined as Epogen, Procrit, Mircera, and Retacrit (biosimilar)

Many Challenges With Biosimilar Adoption Within the Health System

1. Payor coverage
2. Preference of reference biologic due to reimbursement
3. Provider buy-in
4. Patient buy-in
5. Multiple biosimilars
6. Off-label uses
7. Skinny label
8. Lack of interchangeability data
9. Operational infrastructure
10. Chronic vs. Short-term use

Challenges With Biosimilar Adoption Within the Health System

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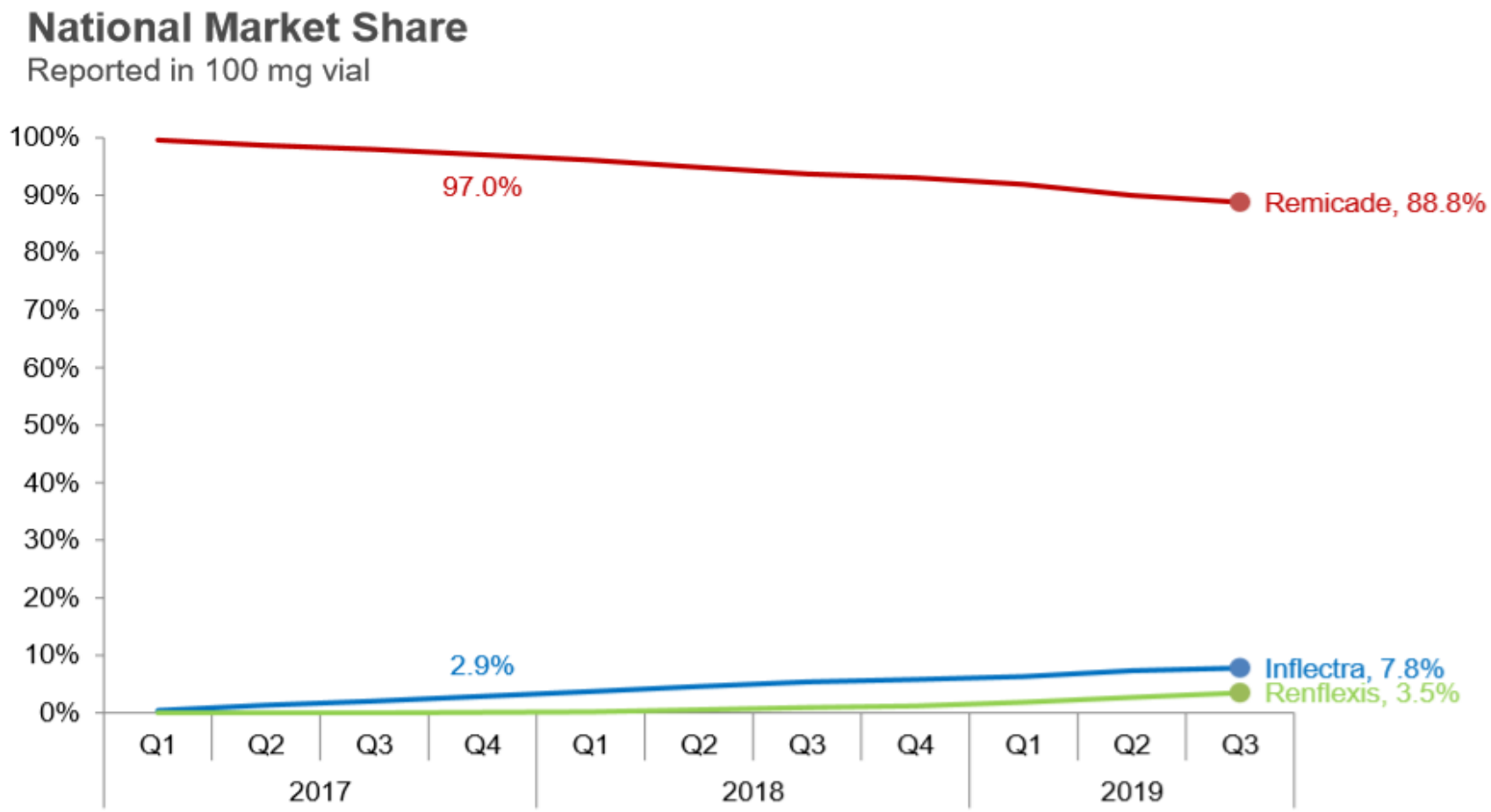
1. Payor Coverage

Nationally, Inflectra® only reached 7.8% of market share in 3rd quarter of 2019



Source: IQVIA DDD data through Q3 2019, reported in 100 mg vial

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2. Preference of Reference Product

Biosimilars absent from chargemaster prices, implying they don't have product available

Academic Medical Ctrs	Neulasta	Remicade	Fulphila	Inflectra	Renflexis
Johns Hopkins	$ 17,263	$ 349			
Mayo Clinic	$ 14,949	$ 305			
NY-Presbyterian	$ 55,239	$ 116			$ 81
UPMC	$ 33,853	$ 700			
UT Southwestern	$ 22,019	$ 1,421		$ 1,898	
Dana-Farber	$ 25,075	$ 833			
Mount Sinai	$ 12,085	$ 244			
UCSF	$ 23,778	$ 687		$ 593	
NorthShore	$ 19,313	$ 250	$ 2,779		
Yale-New Haven	$ 25,089	$ 627			
Vanderbilt	$ 14,268	$ 341		$ 192	
MassGen		$ 269			
UCLA	$ 14,343	$ 318			
Average Charge	$ 23,106	$ 497			
ASP	$ 4,417	$ 72			
Charge Divided by ASP	5.2x	6.9x			

Regional Health Systems	Neulasta	Remicade	Fulphila	Inflectra	Renflexis
Valley Health	$ 28,065	$ 950			
Montefiore Health	$ 24,356	$ 560			
Capital Health	$ 19,542	$ 497			
Adventist Health	$ 11,188	$ 227			
Baptist Health	$ 28,676	$ 497			
Carilion		$ 459			
Saint Francis	$ 13,280	$ 251			
Aspirus	$ 15,341	$ 314		$ 247	
Health Partners	$ 12,363	$ 302			
Avita Health	$ 18,075	$ 339			
Average Charge	$ 18,987	$ 440			
ASP	$ 4,417	$ 72			
Charge Divided by ASP	4.3x	6.1x			

Source: Hospital websites (~40 hospitals were analyzed, but several do not disclose fully); Bernstein analysis; Cells shaded in light red indicate numbers where reporting units are somewhat unclear; ASP data from CMS (Jan 2019 data

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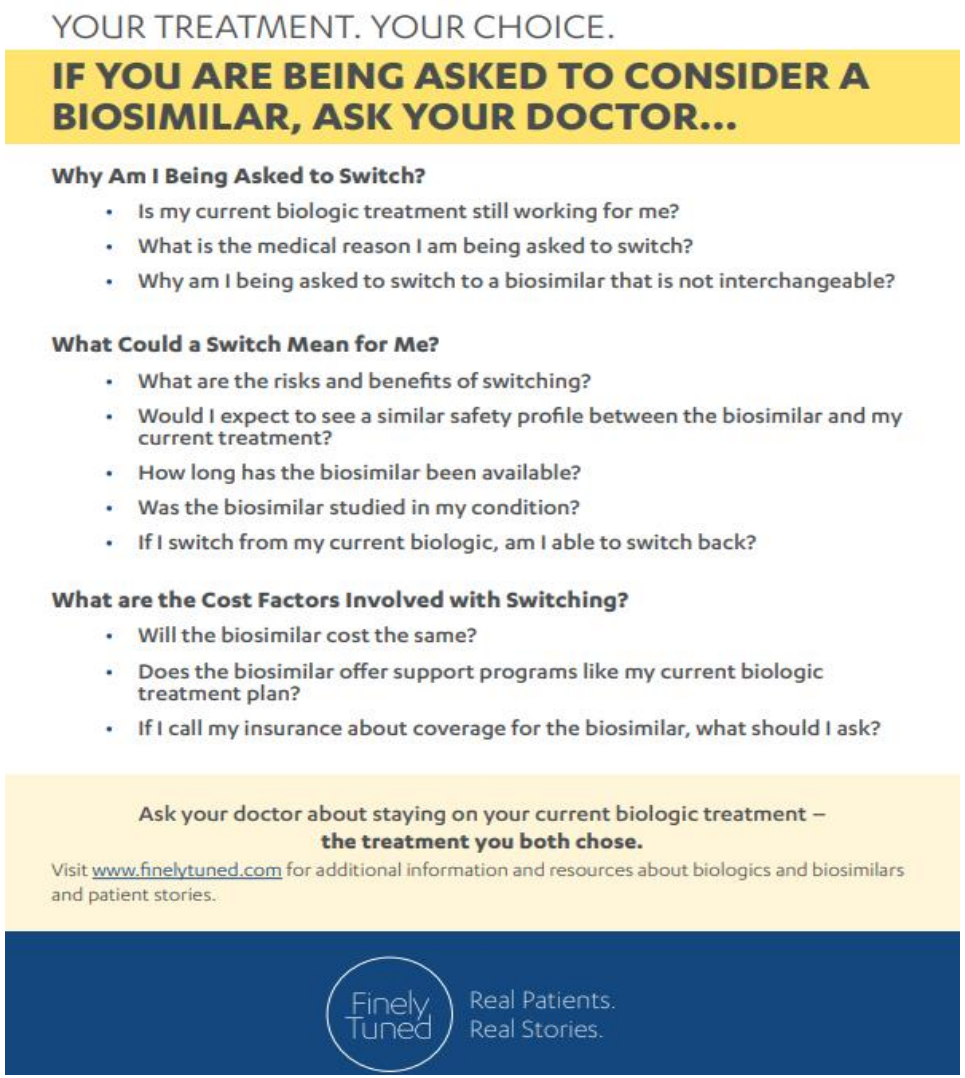
3. Provider Buy-in for Biosimilars

1. Education surrounding biosimilarity pathway
2. Extrapolation of indications
3. Lack of interchangeability
4. Statistical design and power for bio similarity
5. Provider champion (KOL)
6. National guideline support
7. Payor coverage
8. Multi-specialty provider use
9. Pharmacy and nursing support

4. Patient Buy-in for Biosimilars

1. Insurance covers both reference product and biosimilar at parity
2. No difference in cost
3. Long term response to reference product
4. Provider support
5. Lack of education / comprehension of biosimilar vs. reference product
6. Lack of patient advocacy group / disease foundation group support

4. Patient Buy-in for Biosimilars, *continued*



YOUR TREATMENT. YOUR CHOICE.

IF YOU ARE BEING ASKED TO CONSIDER A BIOSIMILAR, ASK YOUR DOCTOR...

Why Am I Being Asked to Switch?

- Is my current biologic treatment still working for me?
- What is the medical reason I am being asked to switch?
- Why am I being asked to switch to a biosimilar that is not interchangeable?

What Could a Switch Mean for Me?

- What are the risks and benefits of switching?
- Would I expect to see a similar safety profile between the biosimilar and my current treatment?
- How long has the biosimilar been available?
- Was the biosimilar studied in my condition?
- If I switch from my current biologic, am I able to switch back?

What are the Cost Factors Involved with Switching?

- Will the biosimilar cost the same?
- Does the biosimilar offer support programs like my current biologic treatment plan?
- If I call my insurance about coverage for the biosimilar, what should I ask?

Ask your doctor about staying on your current biologic treatment – **the treatment you both chose.**

Visit www.finelytuned.com for additional information and resources about biologics and biosimilars and patient stories.

Finely Tuned

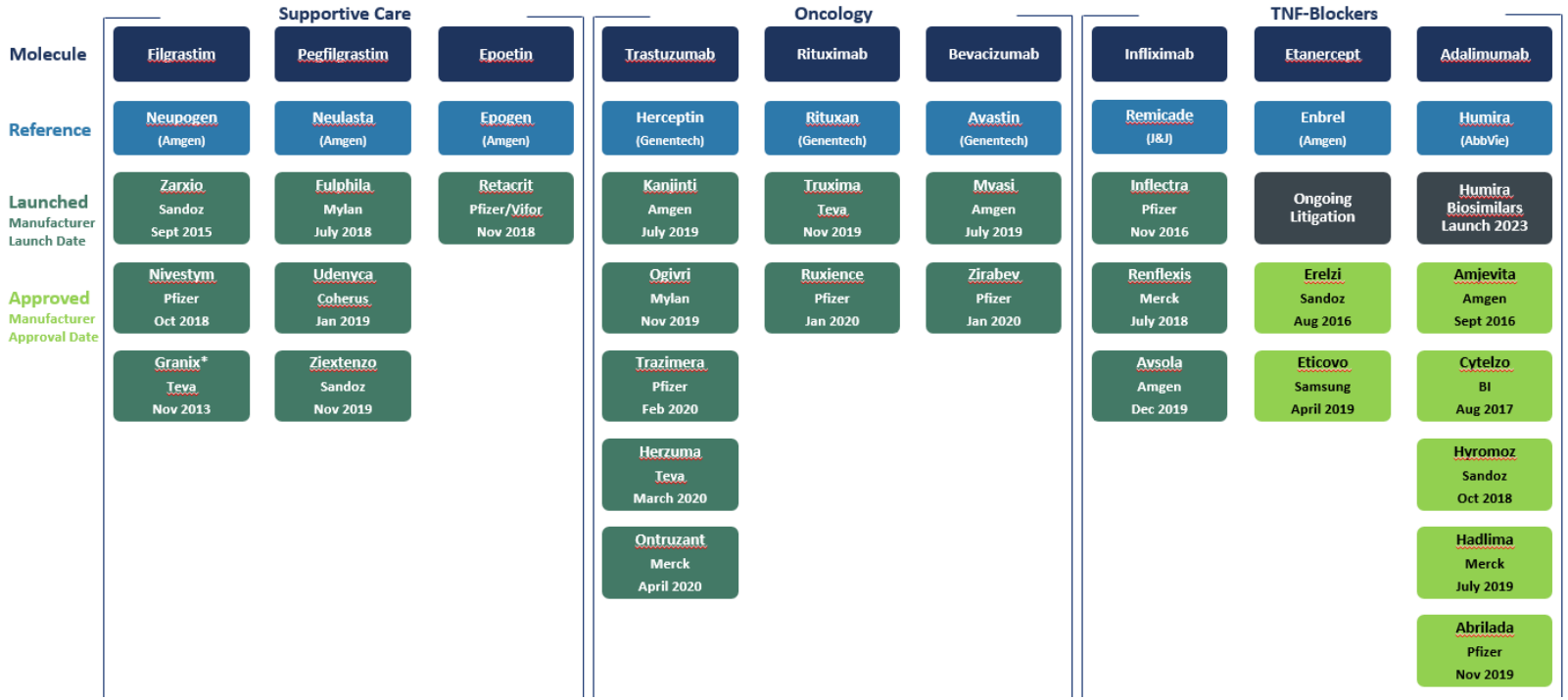
Real Patients.
Real Stories.

Source: Jannsen Biotech Inc., 2018

5. Multiple Biosimilars

Questions to ask:

- Which products have competitive pricing?
- Which biosimilars have robust patient access programs?
- What to do as new biosimilars come out with even more competitive pricing?
- What are the operational impacts? (IT, finance, coverage, nursing ed, inventory)



18 of 25 FDA approved biosimilars have launched

Source: FDA and CDER List of Licensed Biological Products and Fein/Gill/Long Asembia 2019

6. Off-label Use & Coverage of Biosimilars vs. Reference Products

Rituximab®

- Autoimmune thrombocytopenic purpura (ITP)
- Dermatomyositis
- Acute renal rejection
- Systemic lupus erythematosus (SLE)
- Autoimmune encephalitis
- Multiple sclerosis

Remicade®

- Refractory Sarcoidosis
- Sjogren's syndrome
- GVHD
- Vasculitis
- Uveitis

7. Skinny Label Implications

Skinny label – Where biosimilar manufacturers seek approval for only some of the approved indications of a branded drug

Examples

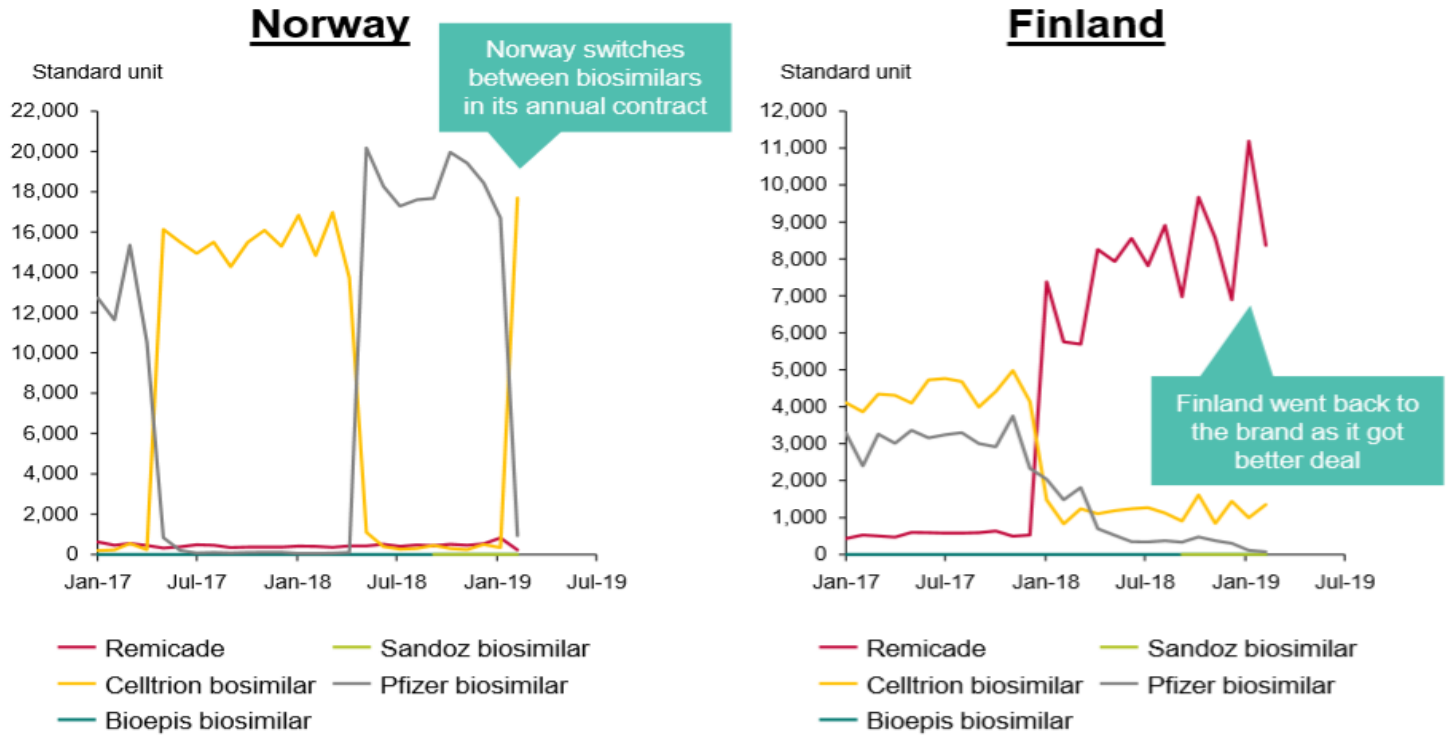
- Truxima® (Rituximab-abbs) only approved for NHL and CLL
- Udenyca® (pegfilgrastim-cbqv) not approved for patients exposed to myelosuppressive doses of radiation
- Implications on practice: Is the product truly not a biosimilar or has a different mechanism of action for those indications so the FDA has not approved it for all indications
- Rationale for skinny label: patent infringement or orphan indication, faster path to distribution

8. Lack of Interchangeability

- Interchangeable product must show that the proposed interchangeable product “can be expected to produce the same clinical result as the reference product in any given patient”
- Based on state regulations, only interchangeable biosimilars can be substituted for reference biologics without provider intervention
- Does non-medical switch = interchangeability ?
- How does state regulations for interchangeability apply to hospital pharmacy?
- https://www.fda.gov/media/124907/download

8. European Interchangeability Experience

Remicade (infliximab) EU market: Scandinavia treating biosimilars as *interchangeable; Norway switched back to Celltrion*



Source: IQVIA; Bernstein analysis

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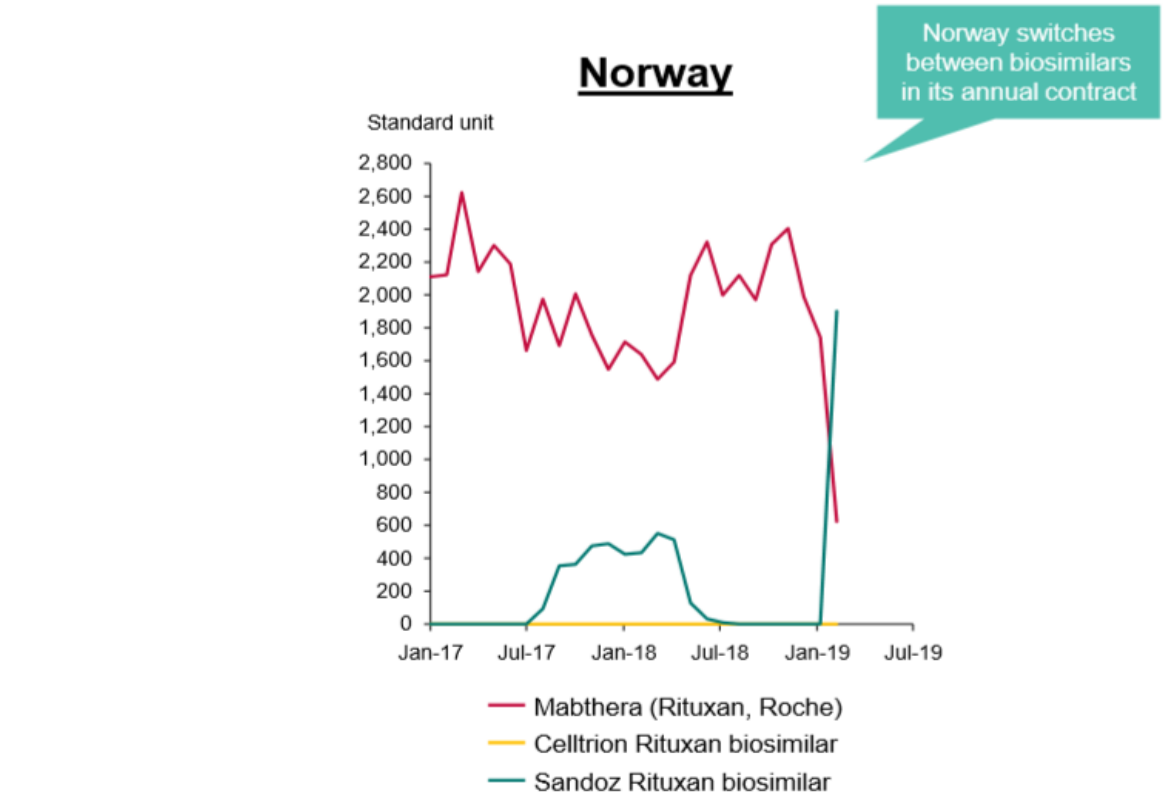
8. EU Interchangeability Experience, *continued*

Rituxan (rituximab) EU market: *Norway switches to Sandoz*



Source: IQVIA; Bernstein analysis

9. Operational Infrastructure

- IT (order sets, billing, coding, modifier)
- Payor coverage assessment
- Patient/Provider/Nursing/Finance education/buy-in/satisfaction
- P&T presentation
- System-wide adoption & consensus
- Contract negotiations
- Inventory management

10. Implications of Chronic vs. Finite Duration of Therapy

Chronic use

- Remicade®
- Herceptin® (MBC)
- Humira®
- Enbrel®
- Rituxan (RA)®
- Procrit®

VS.

Finite # of doses / times used

- Neulasta®
- Herceptin® (Adjuvant)
- Rituxan® (DLBCL)
- Avastin®

Pharmacists Can Help Drive Adoption of Biosimilars

Using a high-touch model for patients to help improve adoption of biosimilars

- Develop patient education material (customized to level of patient health literacy)
- Patient receives educational material prior to any changes
- Patient discusses one-on-one with pharmacist
- Provider may have a touch point before to prime patient of system-wide adoption of biosimilar and their support of it
- Financial implications to healthcare system and patient (per member per month)
- Disease organization/patient advocacy support and education
- Peer-to-peer patient champion
- European/U.S. data (clinical trials, real-world evidence, etc.)

Pathway to Faster Adoption of Biosimilars Within Health Systems

- Biosimilar adoption experience (# of biosimilars adopted)
- Biosimilar pipeline intelligence
- Early contract negotiations
- Payor communication
- Develop P&T approved protocol for newly approved biosimilars – may consider abbreviated pathway
- European provider peer–to-peer connections

Real-world Evidence…

- Kaiser Permanente (KP) with >12M covered lives and largest integrated payor
- 2015 Zarxio® launched
- Sandoz asked KP to name its rebate for 100% conversion rate to Zarxio
- KP physicians questioned European studies
- KP performed its own study on 700 patients and the results showed that neutropenia was lower vs. Filgrastim
- 98% conversion to Zarxio

Source: https://biosimilarsrr.com/2019/11/07/how-did-kaiser-permanente-reach-95-utilization-of-biosimilar-herceptin-and-avastin-so-quickly/ (accessed 1/10/20)

Real-world Evidence Presented at American Society of Hematology

A Retrospective Review of Engraftment Data for Tbo-Filgrastim vs. Filgrastim in Patients Undergoing High Dose Chemotherapy and Autologous Stem Cell Transplantation

Taylor Teschner, Stephen Lo, Dina Brauneis, Anthony Shelton, Bhavesh Shah, J. Mark Sloan, Cindy Varga, Karen Quillen, Vaishali Sanchorawala

In this retrospective chart review, we did not find any significant difference in time to neutrophil engraftment after HDC/SCT when comparing patients who received Filgrastim and then switched to Tbo-Filgrastim after SCT. Even though Tbo-filgrastim is not approved as a biosimilar and lacks interchangeability designation we feel that based on our experience the safety, efficacy and immunogenicity is comparable to filgrastim and there are no clinical meaningful differences between the two products.

Souce: Shah, et al. A Retrospective Review of Engraftment Data for Tbo-filgrastim vs Filgrastim in Patients Undergoing High Dose Chemotherapy and Autologous Stem Cell Transplantation. Presented at American Society of Hematology. Orlando, FL December 2015

2017 KP Inflectra Biosimilar Switch Journey

- Treatment naïve patients utilize electronic medical record to encourage Inflectra® use
- Treatment experienced patients they had providers sign a therapeutic equivalency protocol agreement (signed by Gastroenterology, Dermatology & Rheumatology)
  - Authorizing plan to make the switch
- Patient education and notification letter was sent to each patient signed by their provider
- Clinical pharmacy was utilized to answer patient questions
- Patients were also physically provided education informational handouts at infusion center
- Pharmacy reviewed all patients one week prior to infusion to assure all steps completed
- Nursing protocol and education
- Results no change in efficacy or safety => communicated to all KP providers

Source: https://biosimilarsrr.com/2019/11/07/how-did-kaiser-permanente-reach-95-utilization-of-biosimilar-herceptin-and-avastin-so-quickly/ (accessed 1/10/20)

“Kaiser’s Oncology Biosimilar Journey”…

KP Oncology Biosimilar Journey

- Rapid P&T approval
- Maximized savings by preferring one biosimilar
- “Skinny label” open to approving off-label indications
- Inventory guarantee
- Mvasi,® Kanjinti® and Truxima® are 90%, 85% and 87% (tweet 12/20/19 from Sameer Awsare) in 1 month
- Overall cost savings since 1st biosimilar $200M

Source: https://biosimilarsrr.com/2019/11/07/how-did-kaiser-permanente-reach-95-utilization-of-biosimilar-herceptin-and-avastin-so-quickly/ (accessed 1/10/20)

Boston Medical Center Real-world Evidence Publication JMCP

Process and Clinical Outcomes of a Biosimilar Adoption Program with Infliximab-Dyyb

Shubha Bhat, PharmD, MS,[1] Sarah Altajar, M.D.,[2] Divya Shankar, M.D.,[2] Toni Zahorian, PharmD,[1]

Regine Robert, CPhT,[1] Taha Qazi, M.D.,[3] Bhavesh Shah, RPh,[1] Francis A. Farraye, M.D., MSc[4]

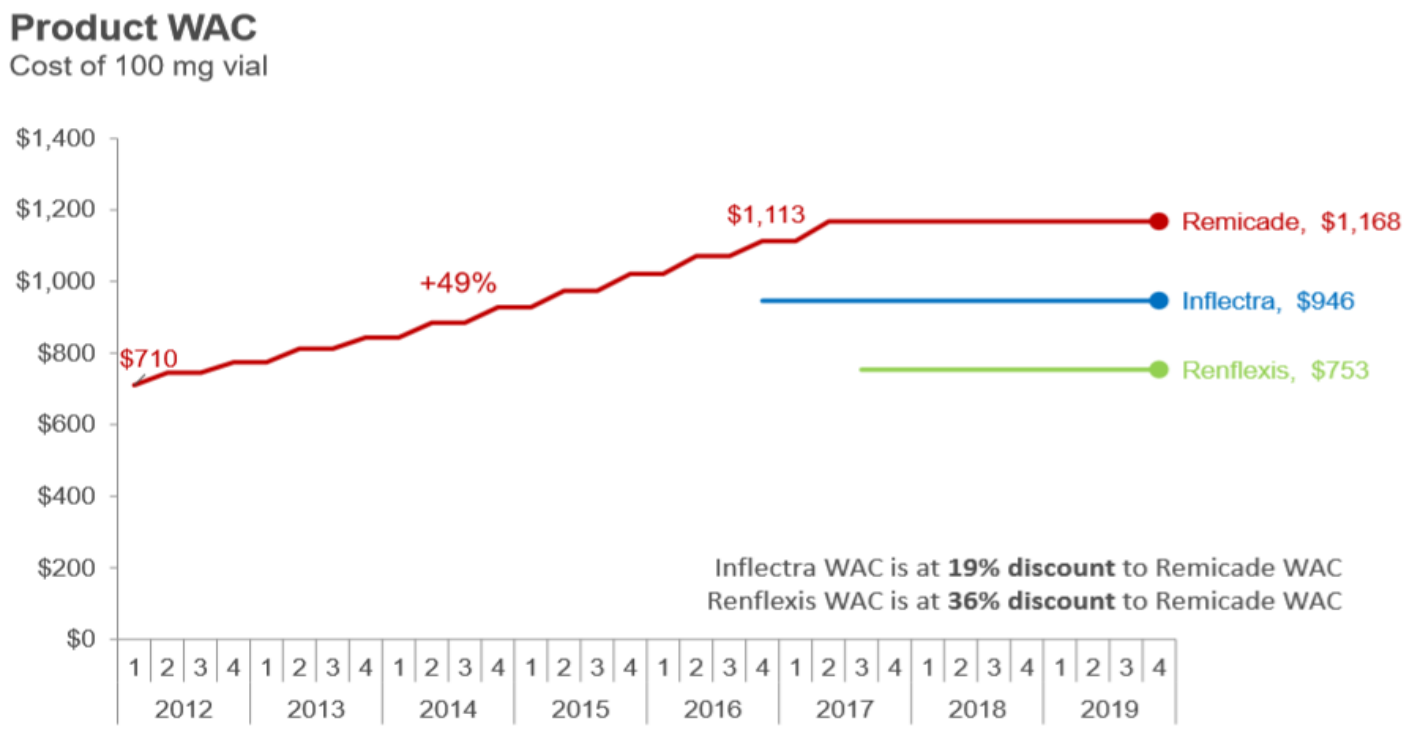
Conclusions

Transitioning patient from IFX to IFX-dyyb can be operationalized at a large scale with 97% conversion rate, which can translate to significant cost savings as long as collaborative efforts between stakeholders are maintained. Payors may present a significant barrier, but emerging real-world data, increase in communication with payors, and future advocacy efforts could bridge that gap. In our assessment of clinical outcomes within the IBD cohort, we found a high proportion of patients transitioned and remained on IFX-dyyb. Additionally, no clinically significant differences in outcomes were seen. The strategies and model used as described in our paper provides a robust biosimilar adoption road map that can be executed at other institutions to increase patient access to biosimilar therapies and generate significant cost-savings to the health care system

Source: Bhat, et al. *J Manag Care Spec Pharm.* 2020;26(4):410-16

Multiple Biosimilar Entrants & Impact on WAC

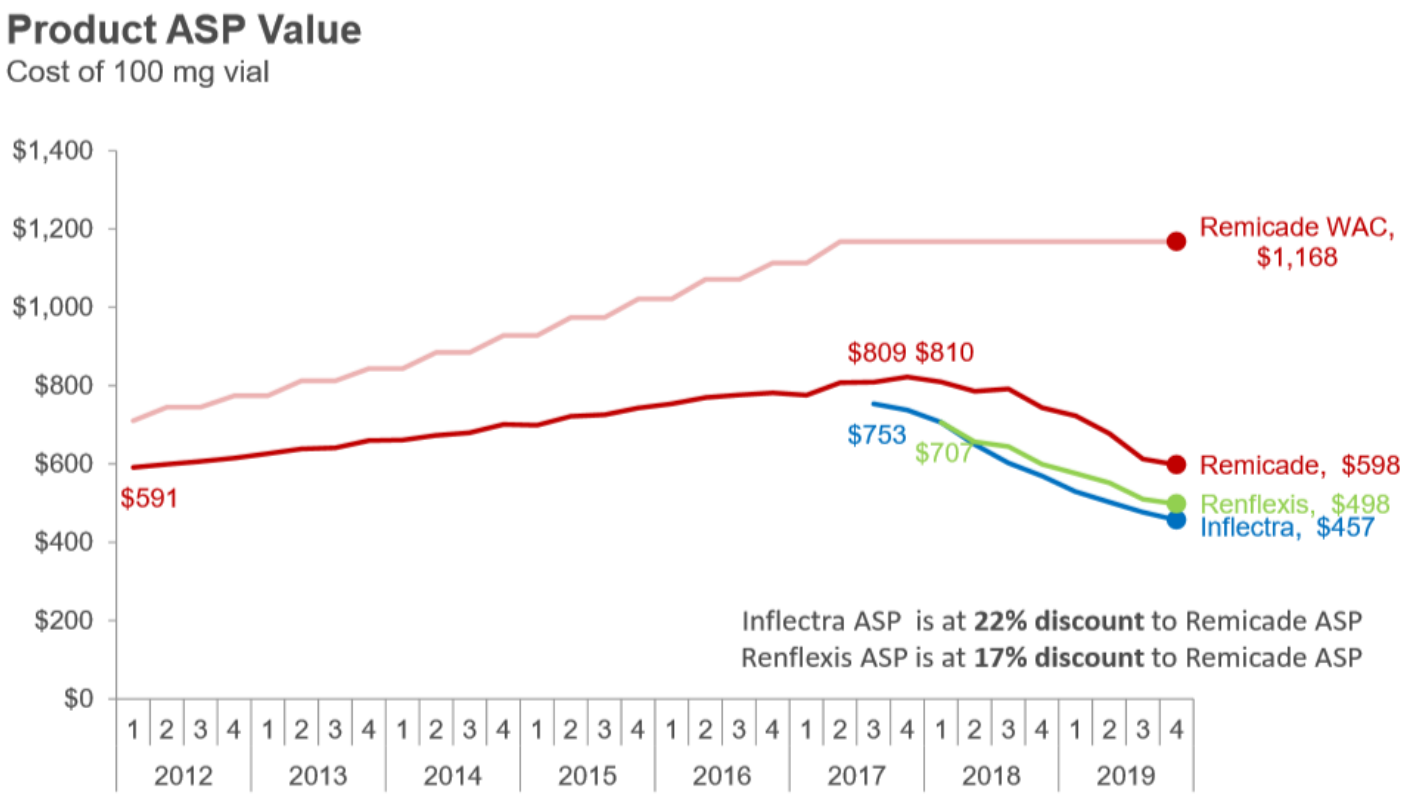
Remicade WAC increased by 49% (from $745 to $1,113) in less than 5 years before the launch of the first biosimilar



Source: Analysource, January 1, 2012 – November 12, 2019

Multiple Biosimilar Entrants & Impact on CMS ASP Pricing

Remicade ASP increased by 37% (from $591 to $809) in less than 5 years before the launch of the first biosimilar



Source: CMS ASP for Q4 2019; All ASPs adjusted to 100 mg

Factors Influencing Cost & Adoption of Biosimilars

The introduction of biosimilars and speed of generics are two factors influencing costs

- **91% of ASHP 2020 panelists indicate biosimilars will achieve 25% market share in the next 5 years**
- **Quote: “This is overly optimistic”**

- **Pacific Research Institute Analysis for Biosimilar Related Cost Savings**
  - The Biosimilar Opportunity Breakdown by state for Medicaid and Commercial market
  - Current use of Biosimilars saves national healthcare system $253.8 million annually relative to an “all originator biologics”
  - Expanding the use of biosimilars in just the nine drug classes where biosimilar competitors are already approved
  - Annual total health care savings of $2.5 billion, $4.8 billion, and $7.2 billion are possible, if their market share grew to 25%, 50% or 75% of the market, respectively

Sources: Vermeulen, et al. Am J Health-Syst Pharm. 2020; 77:84-112
https://www.pacificresearch.org/wp-content/uploads/2019/10/BiosimilarSavings_web.pdf accessed 7/13/20

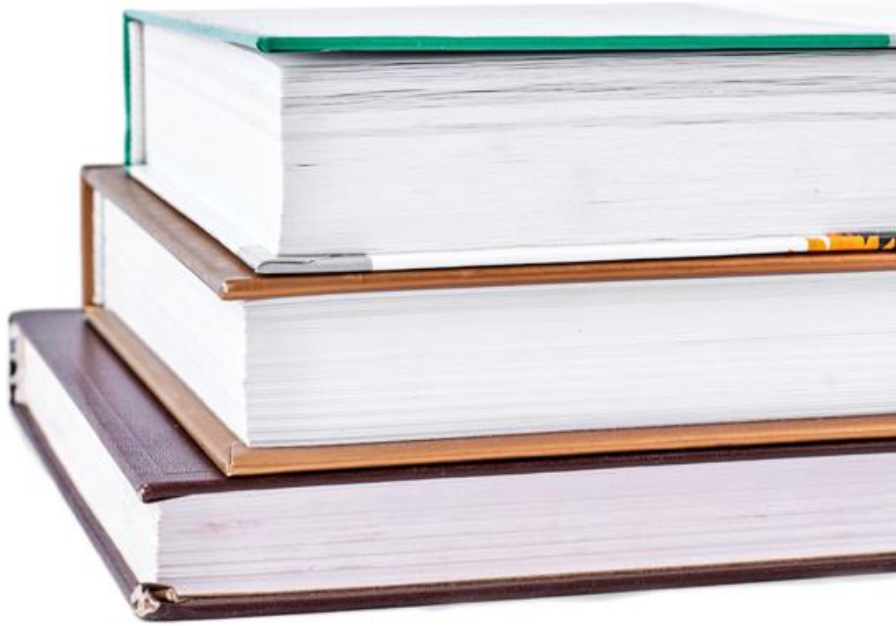
Key Takeaways

- There are 83 biosimilars in development and registered with the FDA for 38 different biologics
- Three biologics which represent $19.4 billion in sales in 2018 will have biosimilars competing for market share
- Based on historical discounts for biosimilars (20% – 30%) and changes in their distribution model potential cost savings of up to $5 billion in 2020 with oncology biosimilars
- Implementing early and aggressive adoptions strategies for the use of biosimilars can lead to major cost savings to U.S. healthcare system
- Questions?

Assessment Question 1

What are factors that limit the cost-savings potential of biosimilars compared to their reference product?

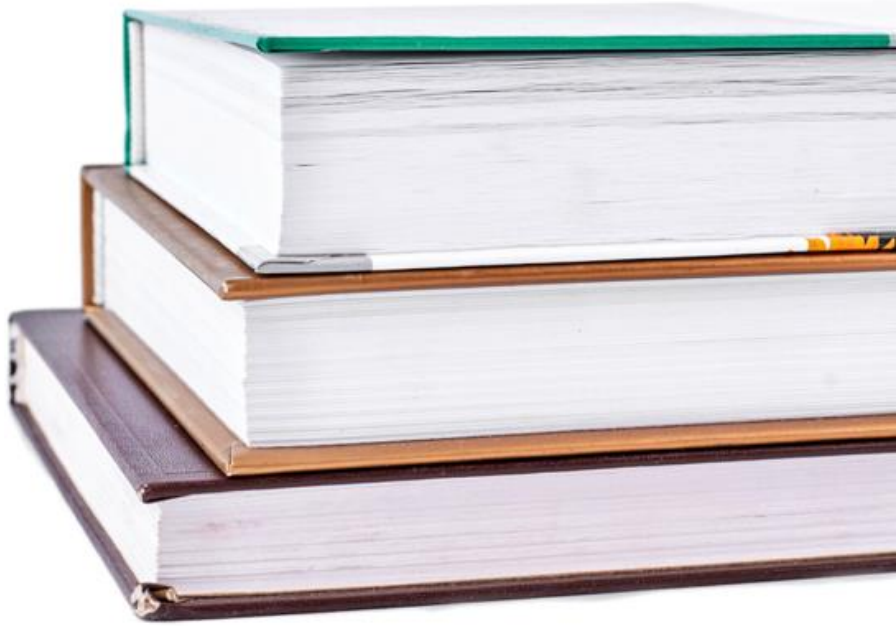
a. Lower reimbursement from payers
b. Provider preference
c. Lack of interchangeability data
d. A and B



Assessment Question 2

Which of the following are areas of concern expressed by health systems related to the adoption of biosimilars?

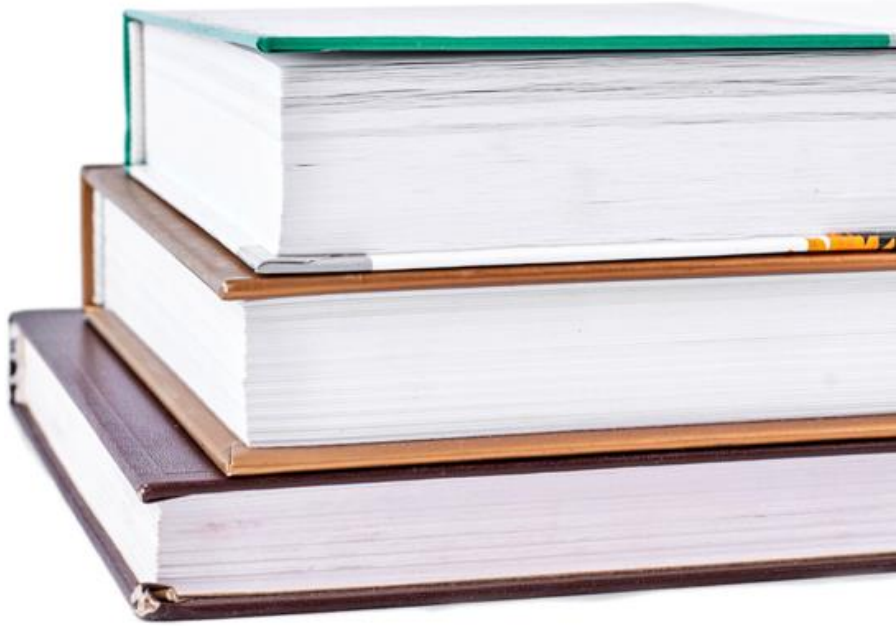
a. Discount from biosimilar too low
b. Patient and provider buy in
c. $100,000 cost to implement biosimilar
d. Payor coverage always favor brand



Assessment Question 3

Which of the following strategies can help improve biosimilar adoption in health systems?

a. Biosimilar adoption is hopeless
b. Government mandate
c. Real world evidence supporting biosimilar switch
d. Interchangeability designation on all biosimilars



References

1. IQVIA Market Prognosis, Sep 2018; IQVIA Institute, Dec 2018.
2. IQVIA Market Prognosis, Dec 2017; IQVIA Institute, Dec 2018.
3. IQVIA Formulary Impact Analyzer; IQVIA Analysis, Dec 2018
4. IQVIA MIDAS, Jun 2018; IQVIA Institute, Dec 2018
5. IQVIA MIDAS, MAT June 2018; ARK Patent Intelligence, IQVIA Institute, Dec. 2018
6. Biosimilars Update: 2019 Report. https://www.amgenbiosimilars.com/pdfs/2019TrendsinBiosimilarsReportElectronicVersionUSA-BIO-80182.pdf. Accessed July 23, 2020.
7. IQVIA, Bernstein analysis.
8. IQVIA DDD data through Q3 2019, reported in 100 mg vial.
9. Jannsen Biotech, Inc., 2018.
10. FDA and CDER List of Licensed Biological Products and Fein/Gill/Long Asembia 2019.
11. FDA. Considerations in demonstrating interchangeability with a reference product: Guidance for industry. https://www.fda.gov/media/124907/download. Accessed July 23, 2020.
12. BR&R Biosimilars Review & Report. How did Kaiser Permanente reach 95%+ utilization of biosimilar Herceptin and Avastin so quickly. https://biosimilarsrr.com/2019/11/07/how-did-kaiser-permanente-reach-95-utilization-of-biosimilar-herceptin-and-avastin-so-quickly/. Accessed July 23, 2020.
13. Bhat et al. Process and clinical outcomes of a biosimilar adoption program with infliximab-dyyb. *J Manag Care Spec Pharm.* 2020;26(4):410-16.
14. Analysource. January 1, 2012 – November 12, 2019.
15. CMS ASP for Q4 2019; all ASPs adjusted to 100 mg.
16. Vermeulen et al. The biosimilar opportunity: A state breakdown. *Am J Health-Syst Pharm*. 2020; 77:84-112. https://www.pacificresearch.org/wp-content/uploads/2019/10/BiosimilarSavings_web.pdf. Accessed July 23, 2020.

Thank you…

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