RhAPP

RHEUMATOLOGY ADVANCED PRACTICE PROVIDERS

4th Annual National Conference

September 21–23, 2023

Biosimilars – Where We Are Today

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Faculty Disclosures

- Tanya Golovanoff, PharmD:
  There are no relevant financial relationships to disclose.
- Steven Sica, PharmD:
  There are no relevant financial relationships to disclose.

Objectives

- Define and differentiate between reference biologic and biosimilar.
- Review the regulation of biosimilars including how biosimilars are created, reviewed, and approved in the United States.
- Discuss concerns about changing between reference biologics and biosimilars.
- Discuss the biosimilar market and list the current biosimilars currently available in Rheumatology

Definitions

Biologic Products:

- Generally large, complex molecules
- Produced through living organisms

Reference Product:

- Biologic product FDA approved whi
  biosimilars are compared to

Biosimilar Product:

- Highly similar and has no **clinically**
  meaningful difference from its refe

Biosimilars: A Review for Health Care Professionals. *FDA.* URL: https://www.fda.gov/drugs/biosimilars/overview-health-care-professionals. Accessed April 2023.

REFERENCE PRODUCT

Original FDA-approved biological product.

Prescribed by a provider.

BIOSIMILAR

Highly similar to and with no clinically meaningful differences from the reference product.

Prescribed by a provider.

INTERCHANGEABLE PRODUCT

Highly similar to and with no clinically meaningful differences from the reference product.

Meets additional requirements.

May be substituted without consulting the prescriber, depending on state pharmacy laws.

Biosimilars: A Review for Health Care Professionals. *FDA.* URL: https://www.fda.gov/drugs/biosimilars/overview-health-care-professionals Accessed 8/8/2023.

What is a Biosimilar?

Determined to have no clinically meaningful difference in sa
potency to the reference product (safe and efficacious)

No clinically meaningful difference is determined by evaluating:

Safety

Purity

Potency

Biosimilar can be approved for indications it was not directly
long as the reference product has the same mechanism, ro

Biologic Product Definitions. *FDA*. URL: https://www.fda.gov/media/108557/download Accessed 8/8/2023

Interchangeable Products

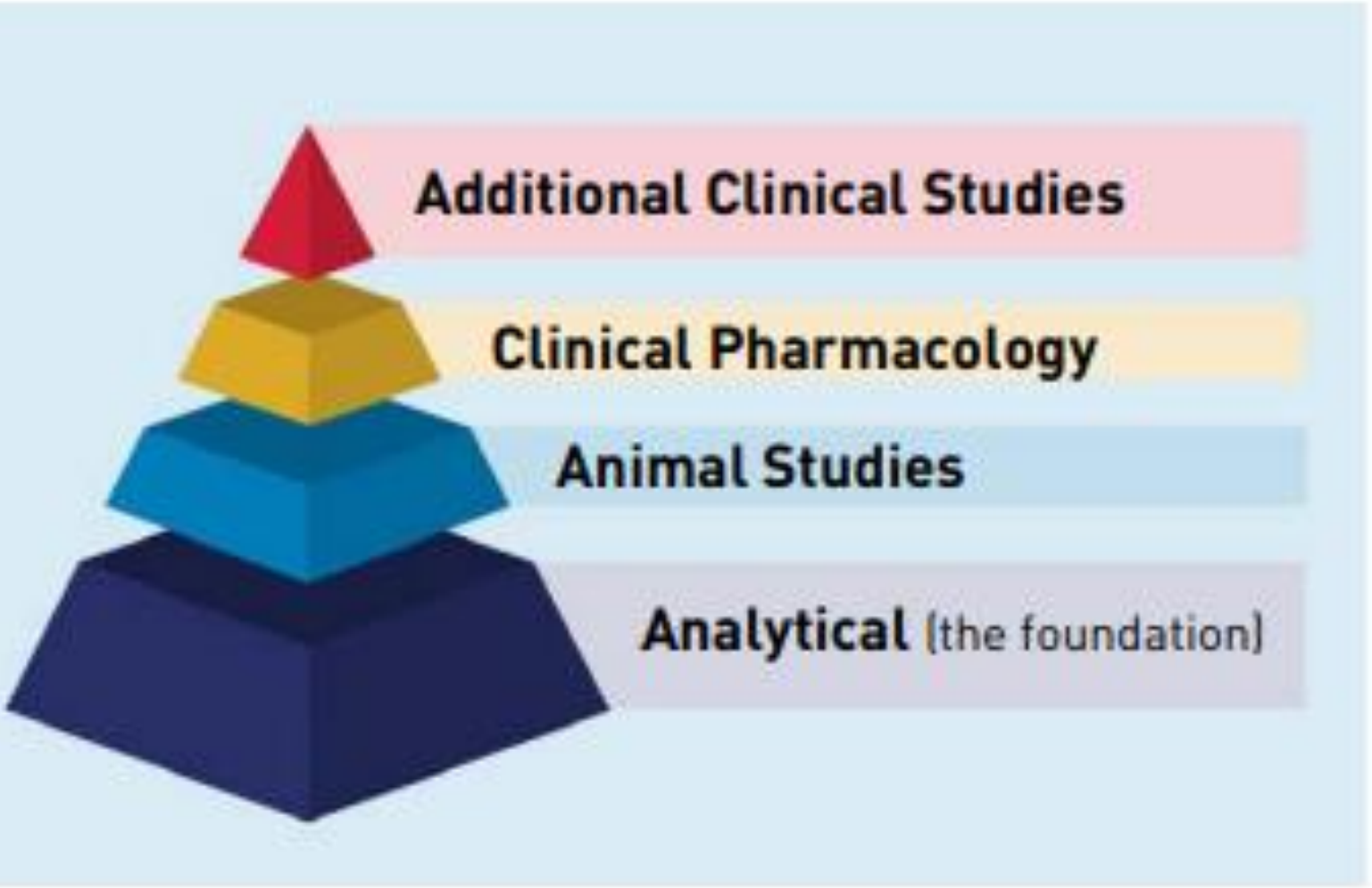
- Biosimilar product which meets additional requirements outlined by the Biologics Price Competition and Innovation Act
- Expected to produce the same clinical result as the reference product for ANY patient
- Interchangeability is an additional approval process sought by the manufacturer
  - Requires “Switching Study”
  - Formulation differences may impact (citrate free vs citrate formulations)

Biologic Product Definitions. *FDA.* URL: https://www.fda.gov/media/108557/download Accessed 8/8/2023.
Biosimilar product regulatory Review and Approval. *FDA.* https://www.fda.gov/media/108621/download. Accessed 8/8/2023

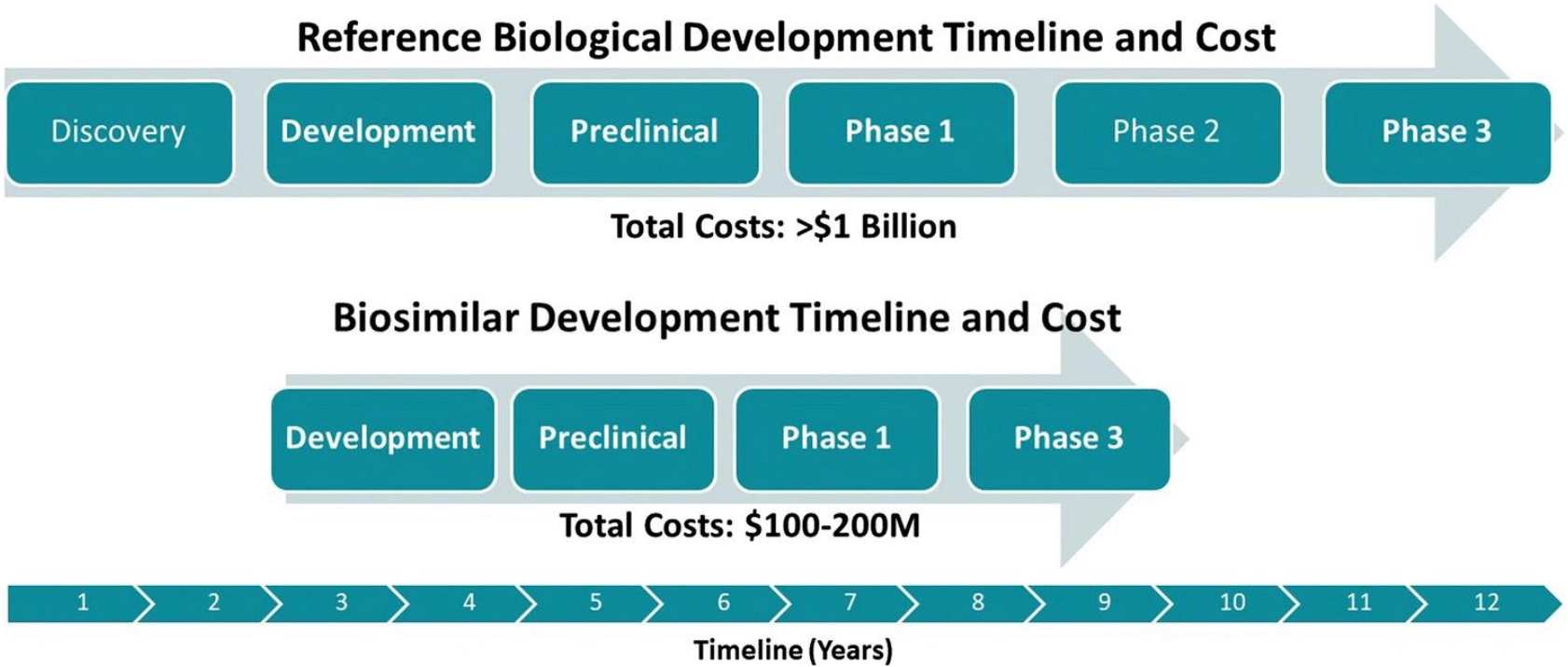
Approval Process of Biosimilars

- Goal of biosimilar development: demonstrate biosimilarity, NOT to independently establish safety and effectiveness of the product
- Manufacturer generates array of data comparing the product to the reference product to demonstrate biosimilarity
- By allowing the manufacturers to focus on similarity instead of treatment studies, this speeds up the process to promote competition and cost savings for patients

Biosimilar product regulatory Review and Approval. *FDA.* https://www.fda.gov/media/108621/download. Accessed 8/8/2023


Additional Clinical Studies
Clinical Pharmacology
Animal Studies
Analytical (the foundation)

Biosimilar Approval Process



Agbogbo, F.K., Ecker, D.M., Farrand, A. *et al.* Current perspectives on biosimilars. *J Ind Microbiol Biotechnol* **46,** 1297–1311 (2019). https://doi.org/10.1007/s10295-019-02216-z
https://biosimilarsrr.com/2020/10/02/us-biosimilar-market-will-soon-catch-up-to-the-eu/

Interchangeable products at the pharmacy

Biosimilars deemed interchangeable are treated similarly to generic drugs

FDA has concluded the medication CAN be substituted at the pharmacy WITHOUT consulting the provider (pending state laws)

Biosimilars that are not interchangeable would need provider consultation prior

Biologic Product Definitions. *FDA.* URL: https://www.fda.gov/media/108557/download Accessed 8/8/2023.

Biosimilars and generics: the same thing?

Similarities

- “Versions” of the brand name (reference product)
- May offer more affordable treatment to patients

Differences

- Generic must demonstrate bioequivalence
- Biosimilars must demonstrate high similarity to reference product and must demonstrate NO clinically meaningful differences in safety and efficacy

Biologic Product Definitions. *FDA.* URL: https://www.fda.gov/media/108557/download Accessed 8/8/2023.

Naming Biosimilars

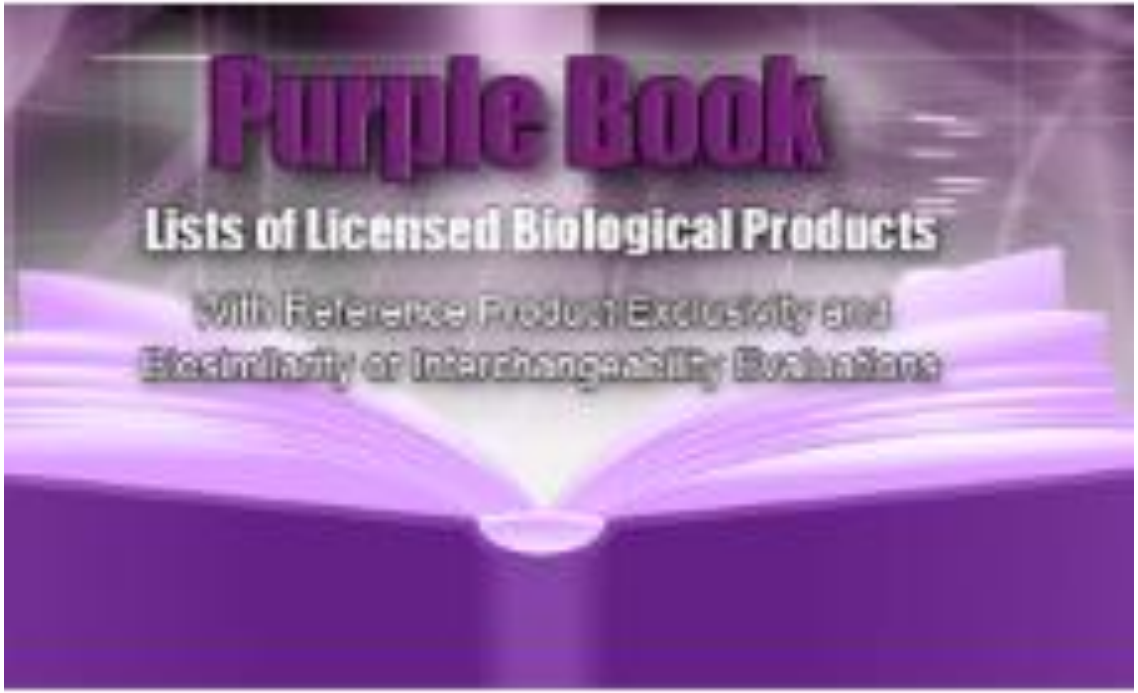
FDA Guidance for industry in January 2017

Must bear a non-proprietary name that includes and FDA-designated suffix

Non-proprietary name used is that of the originator biologic product, which contains the core name and a distinguishing suffix that is devoid of meaning and composed of four lowercase letters

What should patients know?

- Biologics are made from the same source as reference product
  - Similar to loaves of bread
- Clinically considered the same as reference product
  - No expected differences in risks or benefits
- FDA goes through EXTENSIVE investigation of these products to meet standards
- Lower cost does not reflect quality or effectiveness


Purple Book
Lists of Licensed Biological Products

Adalimumab (Humira) Biosimilars

adalimumab

Abrilada (adalimumab-afzb) **BLA Number:** 761118	*351(k) Biosimilar*
Amjevita (adalimumab-atto) **BLA Number:** 761024	*351(k) Biosimilar*
Cyltezo (adalimumab-adbm) **BLA Number:** 761058	*351(k) Interchangeable*
Hadlima (adalimumab-bwwd) **BLA Number:** 761059	*351(k) Biosimilar*
Hulio (adalimumab-fkjp) **BLA Number:** 761154	*351(k) Biosimilar*
Humira (adalimumab) **BLA Number:** 125057	*351(a)*
Hyrimoz (adalimumab-adaz) **BLA Number:** 761071	*351(k) Biosimilar*
Idacio (adalimumab-aacf) **BLA Number:** 761255	*351(k) Biosimilar*
Yuflyma (adalimumab-aaty) **BLA Number:** 761219	*351(k) Biosimilar*
Yusimry (adalimumab-aqvh) **BLA Number:** 761216	*351(k) Biosimilar*

Advanced Search

Database last updated: July 25, 2023

Adalimumab-adbm (Cyltezo)

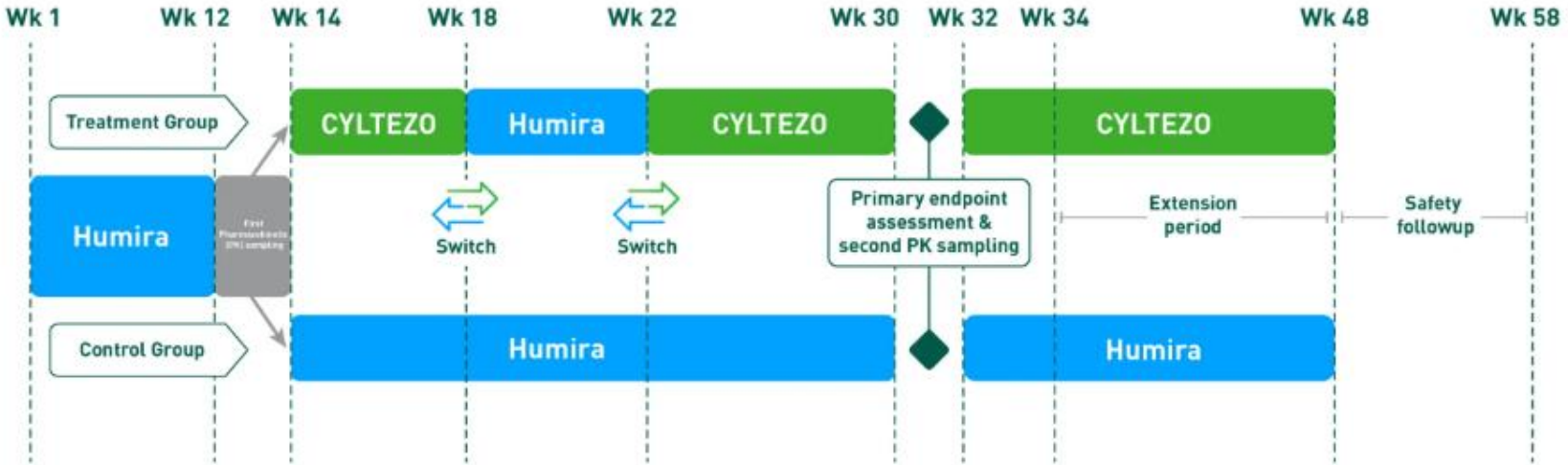
- Only biosimilar for adalimumab considered to be interchangeable
- Second product to receive this designation (insulin glargine)
- Other manufacturers have applied for interchangeability but are pending review still

Cyltezo Switch Study (VOLTAIRE-X)

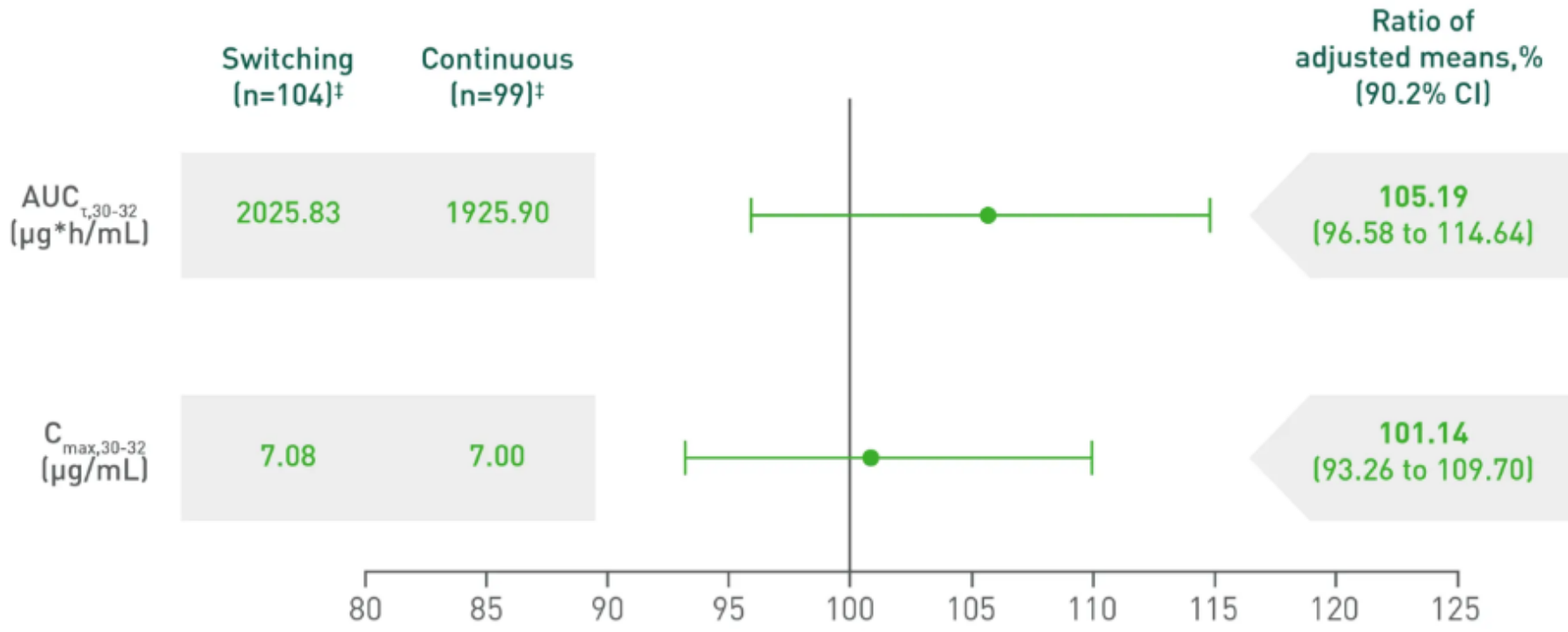
- Patients age 18 to 80 diagnosed with moderate to severe chronic plaque psoriasis with stable disease

- After 14 weeks of treatment with Humira, patients either received Humira or switched to Cyltezo, back to Humira then back to Cyltezo

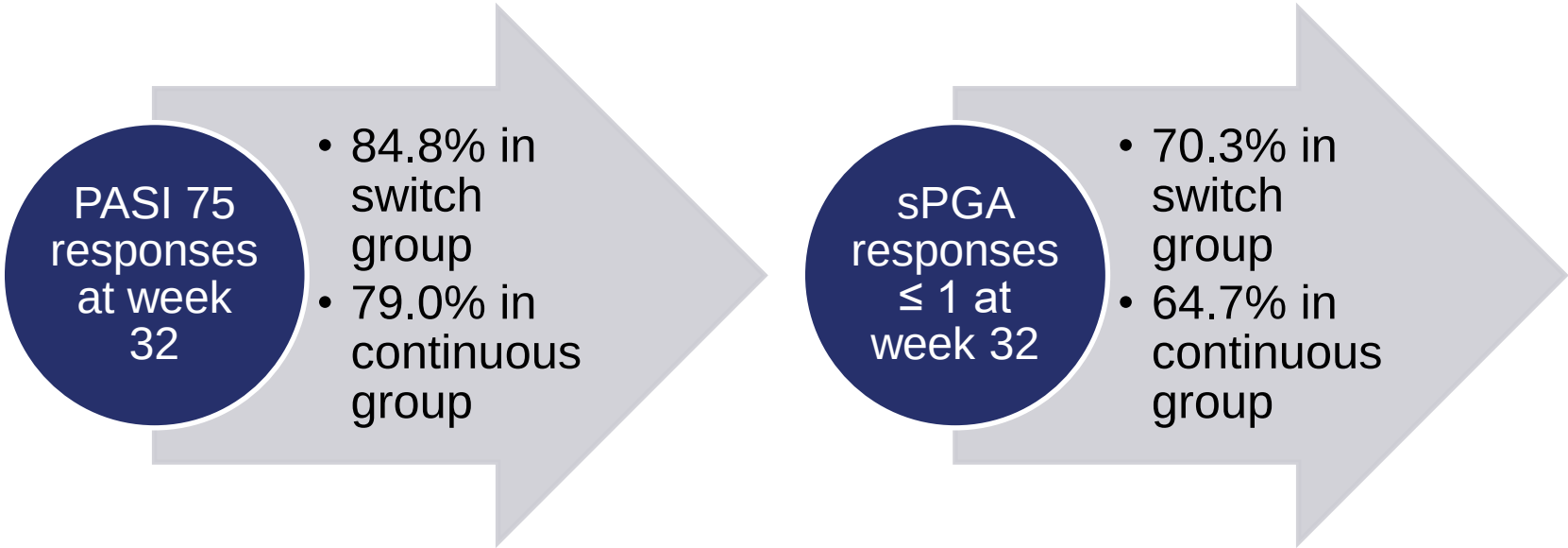
Menter A, Cohen S, Kay J, et al. Switching Between Adalimumab Reference Product and BI 695501 in Patients with Chronic Plaque Psoriasis (VOLTAIRE-X): A Randomized Controlled Trial. Am J Clin Dermatol. 2022 Sep;23(5):719-728. doi: 10.1007/s40257-022-00708-w. Epub 2022 Aug 7. PMID: 35934770; PMCID: PMC9464749.


Wk 1
Wk 12
Wk 14
Wk 18
Wk 22
Wk 30
Wk 32
Wk 34
Wk 48
Wk 58
Treatment Group
Humira
Control Group
CYLTEZO
Humira
CYLTEZO
CYLTEZO
Switch
Switch
Primary endpoint assessment & second PK sampling
Extension period
Safety followup
Humira
Humira

Primary endpoints of the switching study: Humira vs CYLTEZO



Efficacy



Menter A, Cohen S, Kay J, et al. Switching Between Adalimumab Reference Product and BI 695501 in Patients with Chronic Plaque Psoriasis (VOLTAIRE-X): A Randomized Controlled Trial. Am J Clin Dermatol. 2022 Sep;23(5):719-728. doi: 10.1007/s40257-022-00708-w. Epub 2022 Aug 7. PMID: 35934770; PMCID: PMC9464749.

Safety

Safety summary post-randomization (safety evaluation set)

Adverse events, n (%)	Switching (n=118)	Continuous (n=120)	Total (n=238)
At least one treatment-emergent adverse event (TEAE)	67 (56.8)	75 (62.5)	142 (59.7)
At least one TEAE¶	14 (11.9)	22 (18.3)	36 (15.1)
At least one serious TEAE	5 (4.2)	4 (3.3)	9 (3.8)
At least one non-serious TEAE	67 (56.8)	72 (60.0)	139 (58.4)
At least one serious TEAE¶	0 (0.0)	1 (0.8)	1 (0.4)
At least one severe TEAE	3 (2.5)	5 (4.2)	8 (3.4)
At least one TEAE of special interest#	1 (0.8)	0 (0.0)	1 (0.4)
TEAE leading to discontinuation	1 (0.8)	2 (1.7)	3 (1.3)

¶Investigator-assessed.
#Defined as hepatic injury, anaphylactic reactions, serious infection, or hypersensitivity reactions.

Biosimilar Landscape

Social and Economic Challenges

- Population is aging → rising prevalence of Chronic Conditions
- Global spending on pharmaceutical products continues to increase
- Biologics are an important but expensive portion of new drugs

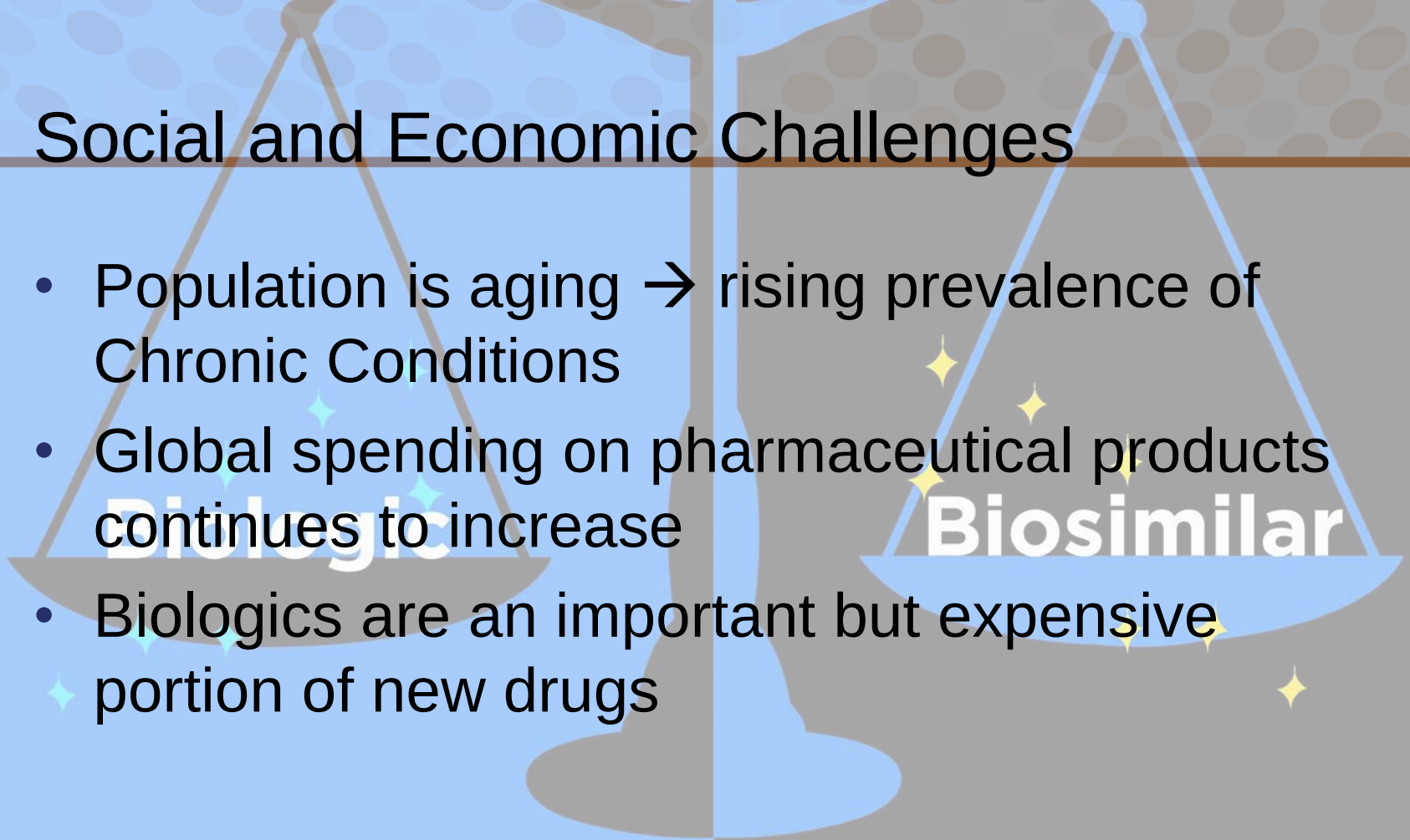
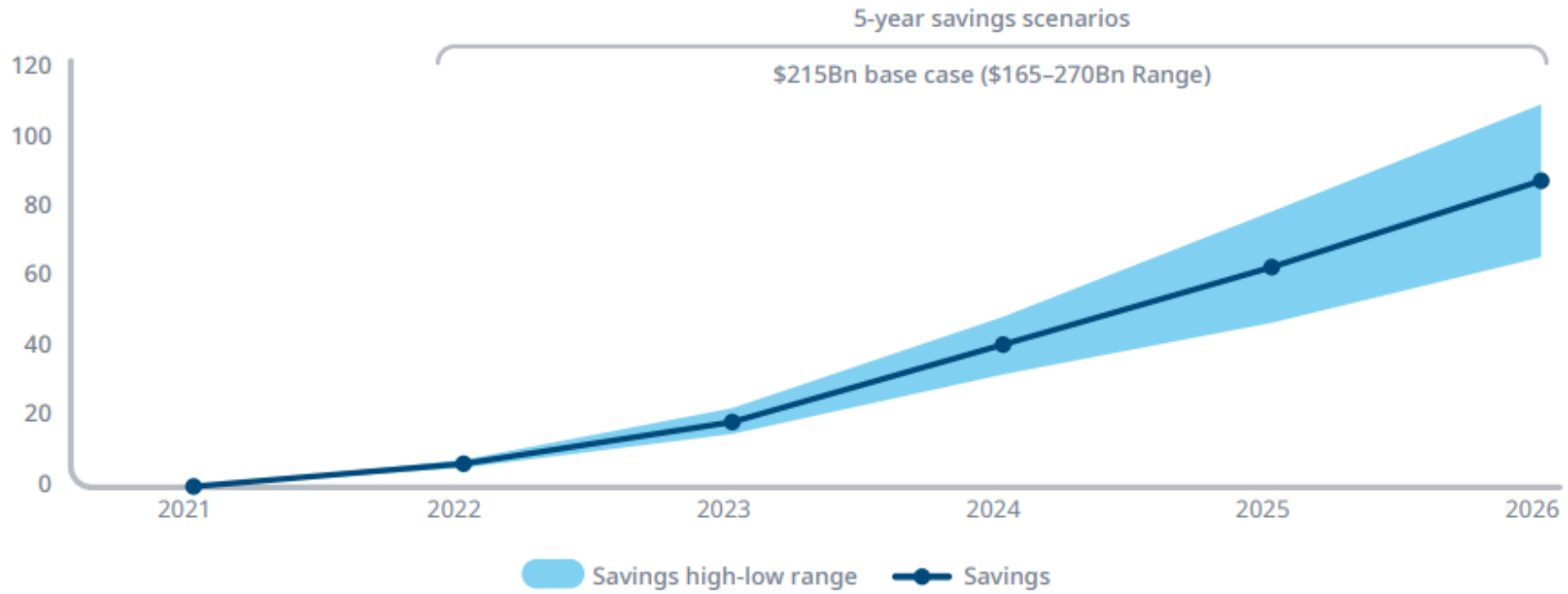
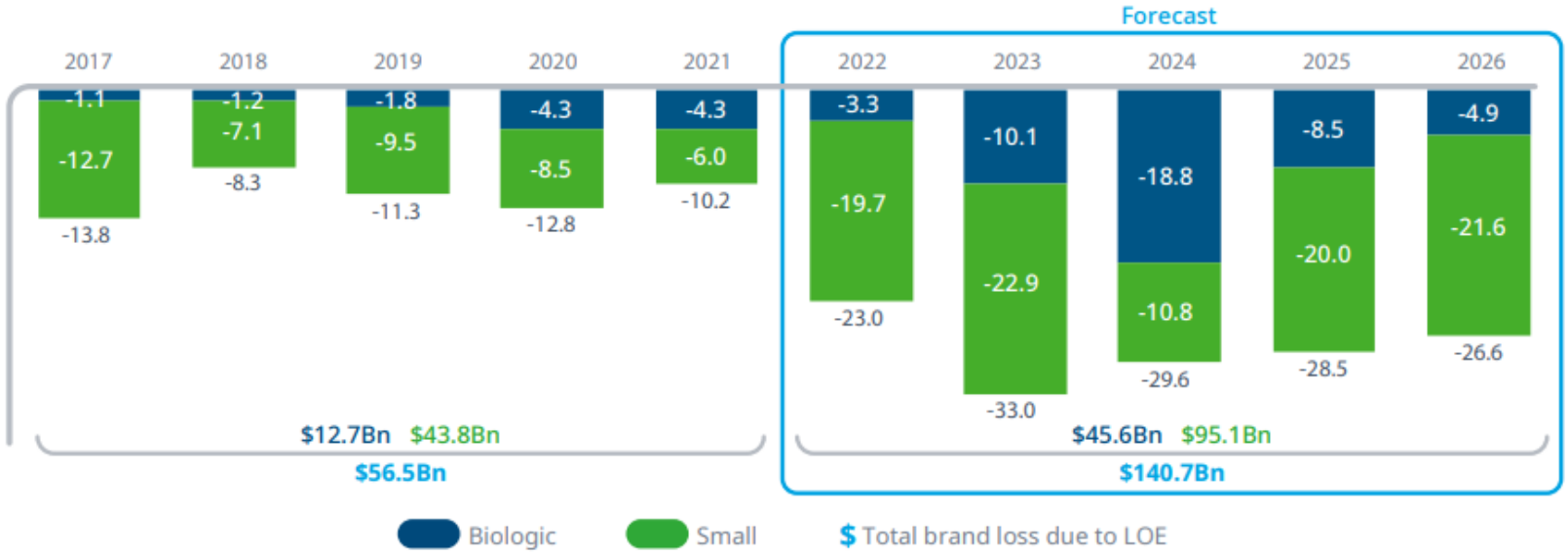


Exhibit 39: Global savings from biosimilars 2021–2026



Source: IQVIA Market Prognosis, Sep 2020; IQVIA Institute Mar 2021

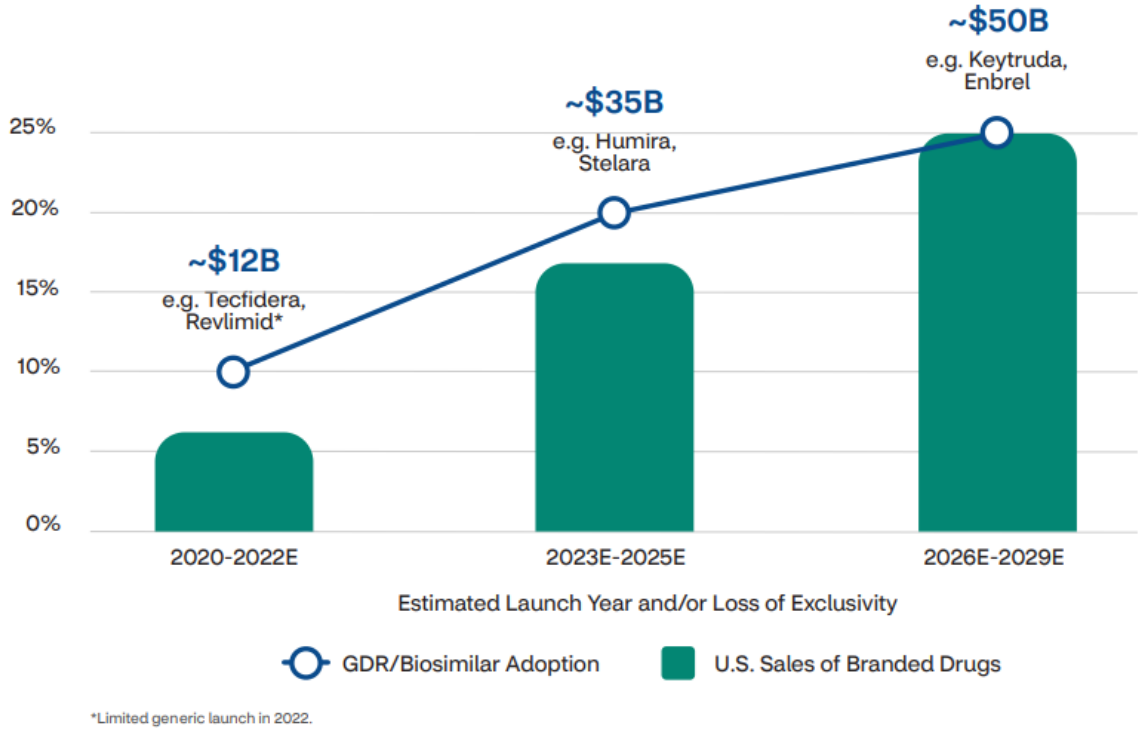
Exhibit 25: U.S. Impact of brand losses of exclusivity 2017–2026, US$Bn



Source: IQVIA Market Prognosis, Sep 2021; IQVIA Institute, Nov 2021

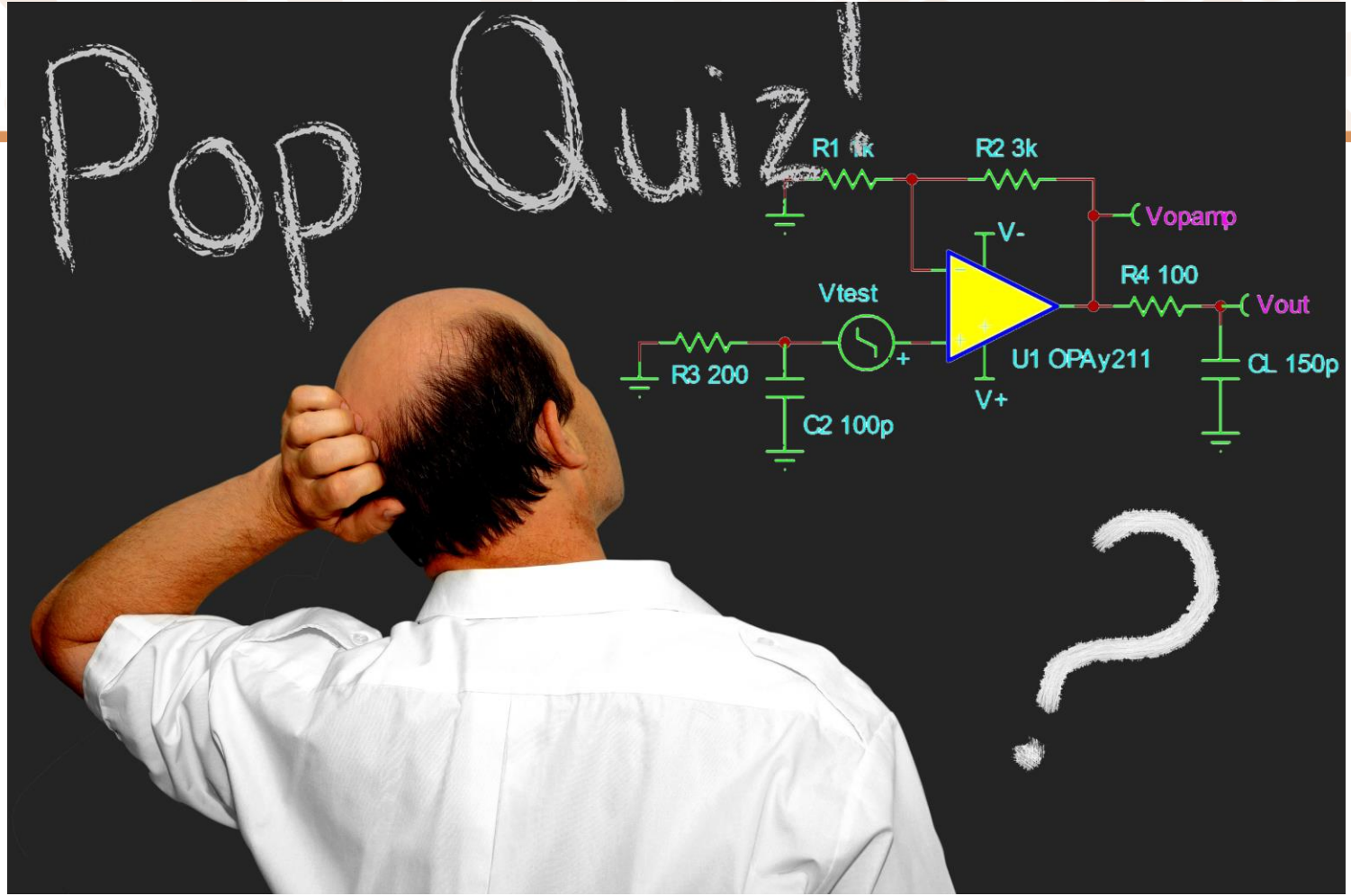
Projected U.S. Market Impact of Generic/Biosimilar Competition on Top Specialty Branded Products

U.S. Market Sales, Illustrative Not Exhaustive

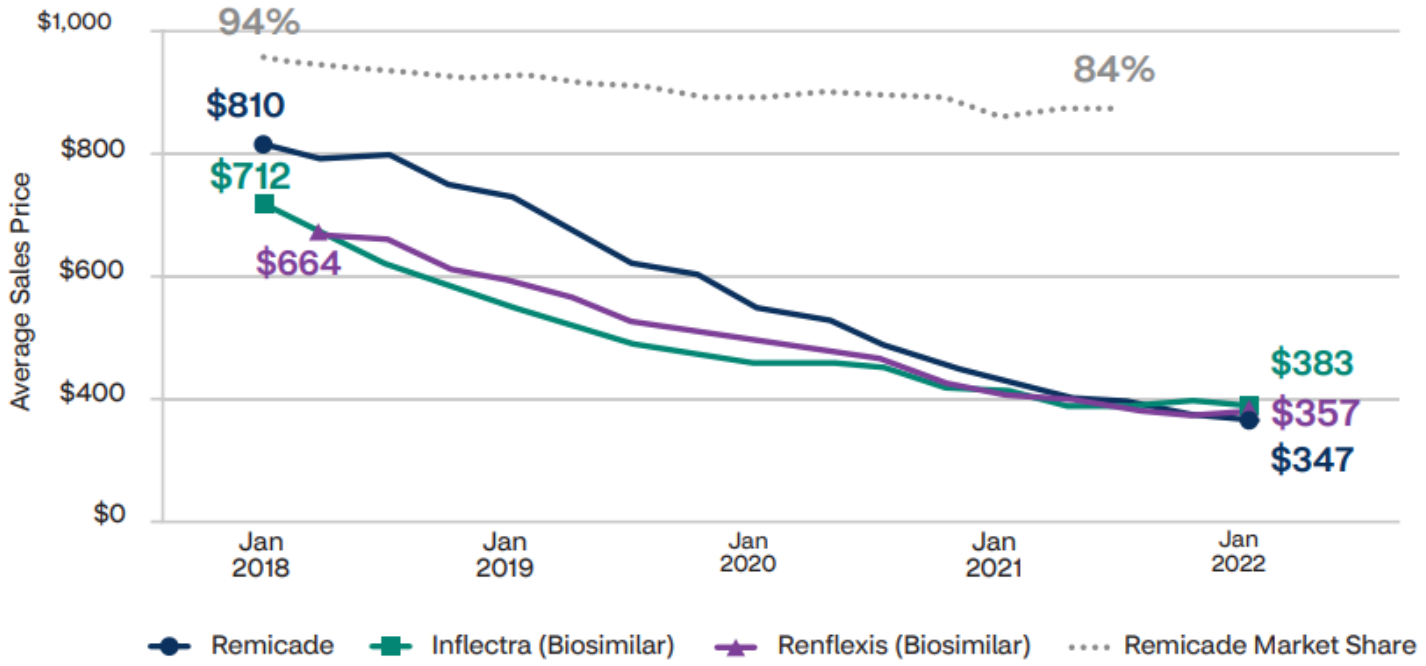


*Limited generic launch in 2022.

[The Drug Trend Report: 2021 Cost Savings Data (cvshealth.com)]


Pop Quiz!
R1 1k
R2 3k
Voparmp
V-
R4 100
Vout
Vtest
R3 200
U1 OPAy211
CL 150p
C2 100p
V+

Infliximab Average Sales Price (ASP) Evolution from 2018-2022

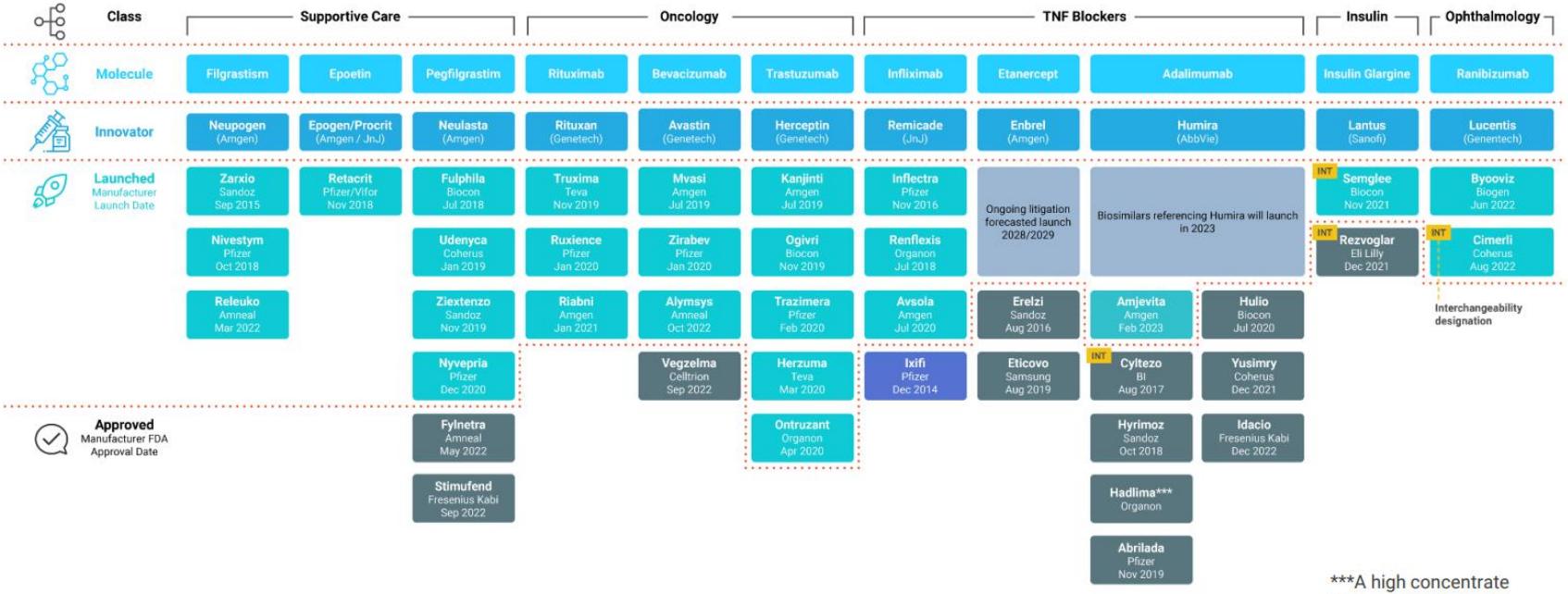


The Drug Trend Report: 2021 Cost Savings Data (cvshealth.com)

U.S. Biosimilars Market Landscape

As of February 2023

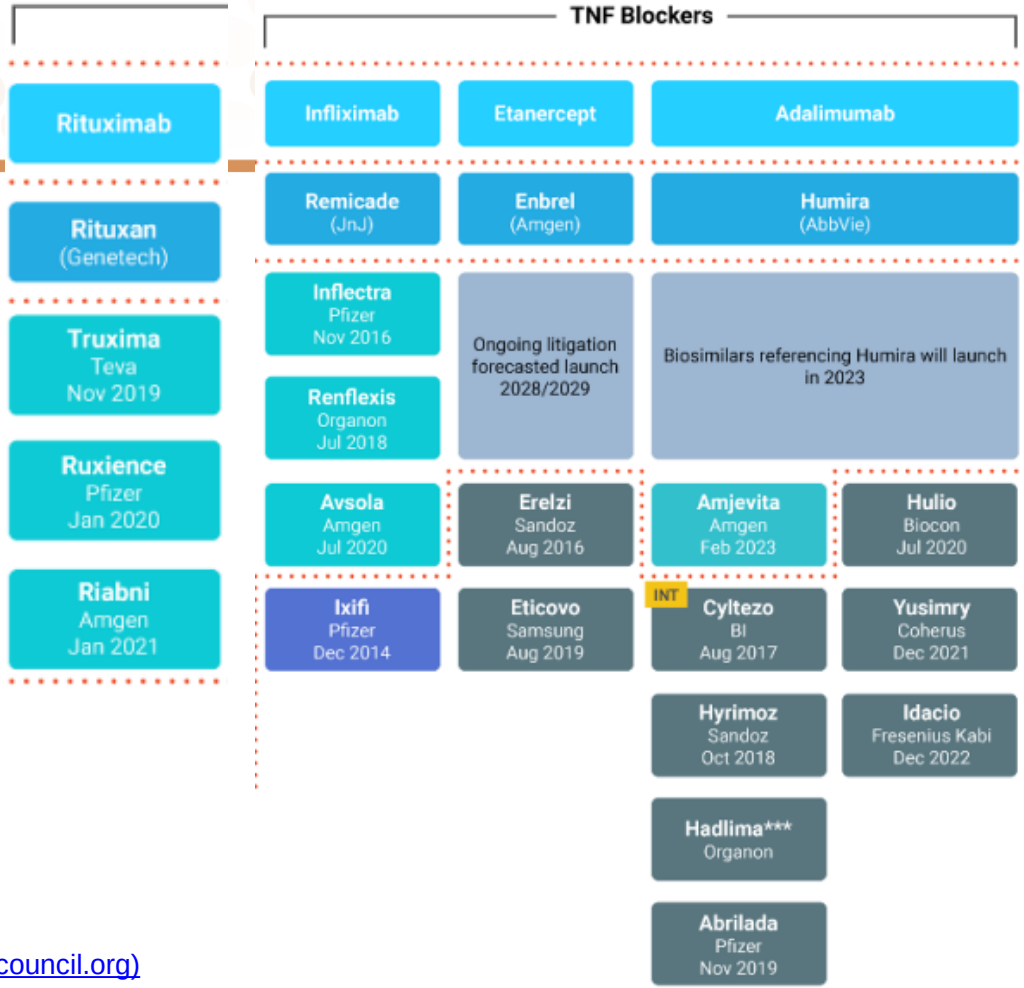
BIOSIMILARS COUNCIL™ A DIVISION OF AAM



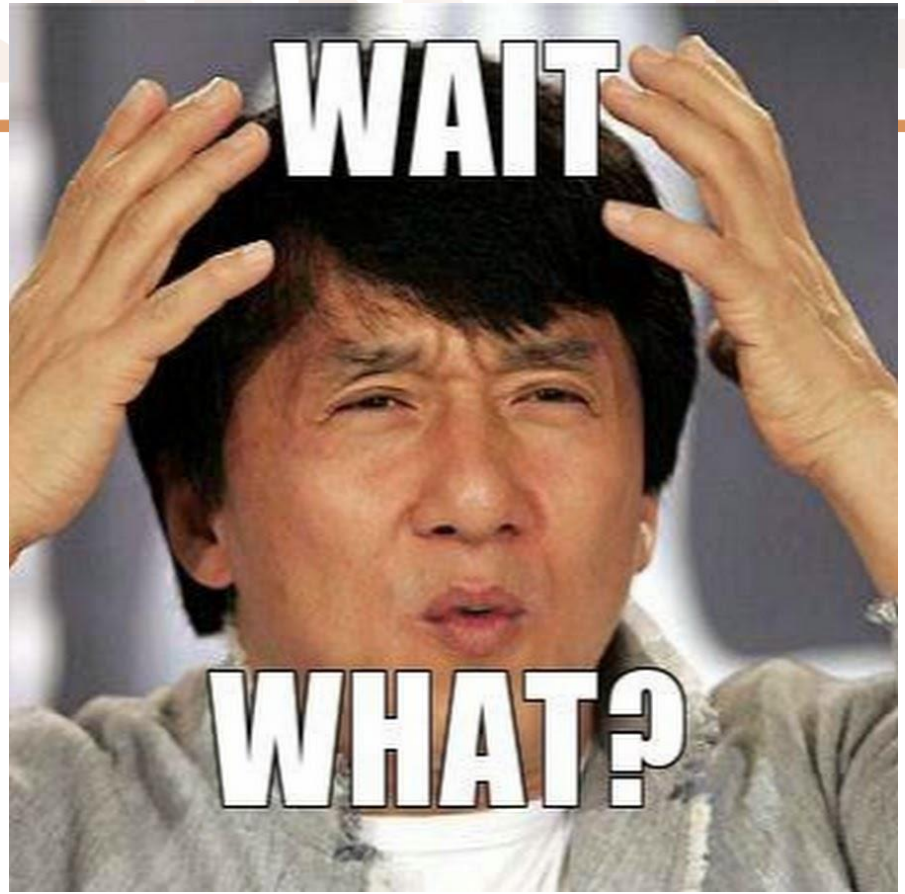
***A high concentrate (August 2022) and low concentrate (July 2019) version are approved

US-biosimilars-market-landscape-2023-02.pdf (biosimilarscouncil.org)

Rheumatology Relevant Biosimilar Market



US-biosimilars-market-landscape-2023-02.pdf (biosimilarscouncil.org)



Adalimumab

Humira
(AbbVie)

Biosimilars referencing Humira will launch in 2023

Amjevita
Amgen
Feb 2023

Hulio
Biocon
Jul 2020

INT

Cyltezo
BI
Aug 2017

Yusimry
Coherus
Dec 2021

Hyrimoz
Sandoz
Oct 2018

Idacio
Fresenius Kabi
Dec 2022

Hadlima***
Organon

Abrilada
Pfizer
Nov 2019

All Eyes on Adalimumab

Global Sales of Humira since 2003

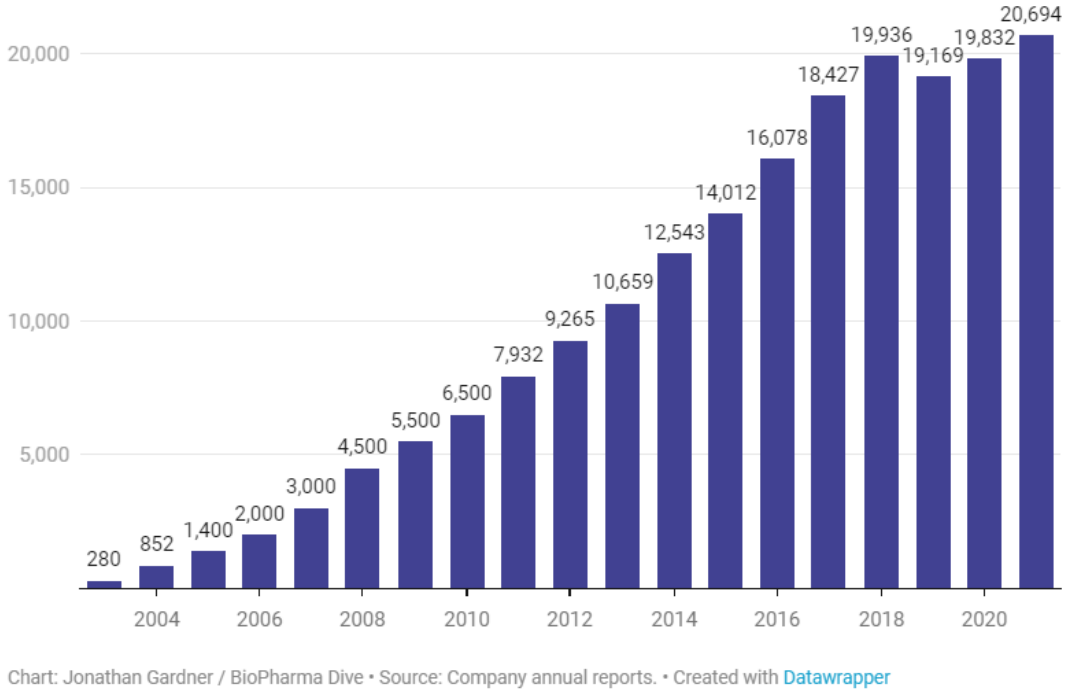


Chart: Jonathan Gardner / BioPharma Dive • Source: Company annual reports. • Created with Datawrapper

Humira is the highest-selling pharmaceutical product in history, earning nearly $200 billion since its late 2002 U.S. approval.

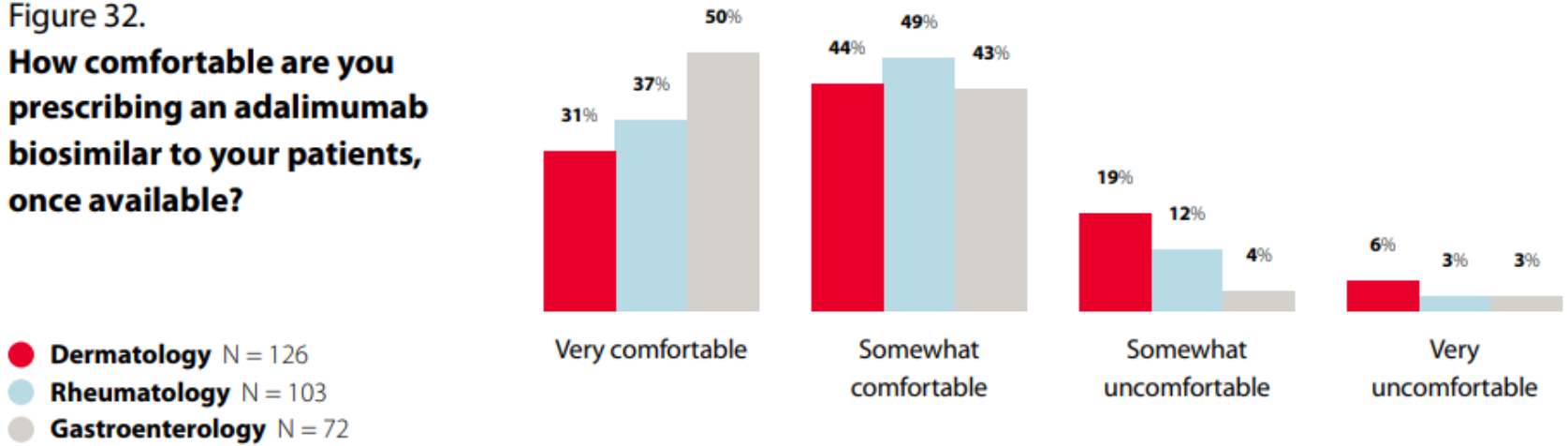
(Figures in millions of dollars)

Two decades and $200 billion: AbbVie's Humira monopoly nears its end | BioPharma Dive


WHOA!
THAT'S A LOT OF MONEY

Figure 32.

How comfortable are you prescribing an adalimumab biosimilar to your patients, once available?



[Preview: 2023 Biosimilars Report (cardinalhealth.com)]

Figure 39.

What are your top concerns regarding adalimumab biosimilars? Please select up to 3.

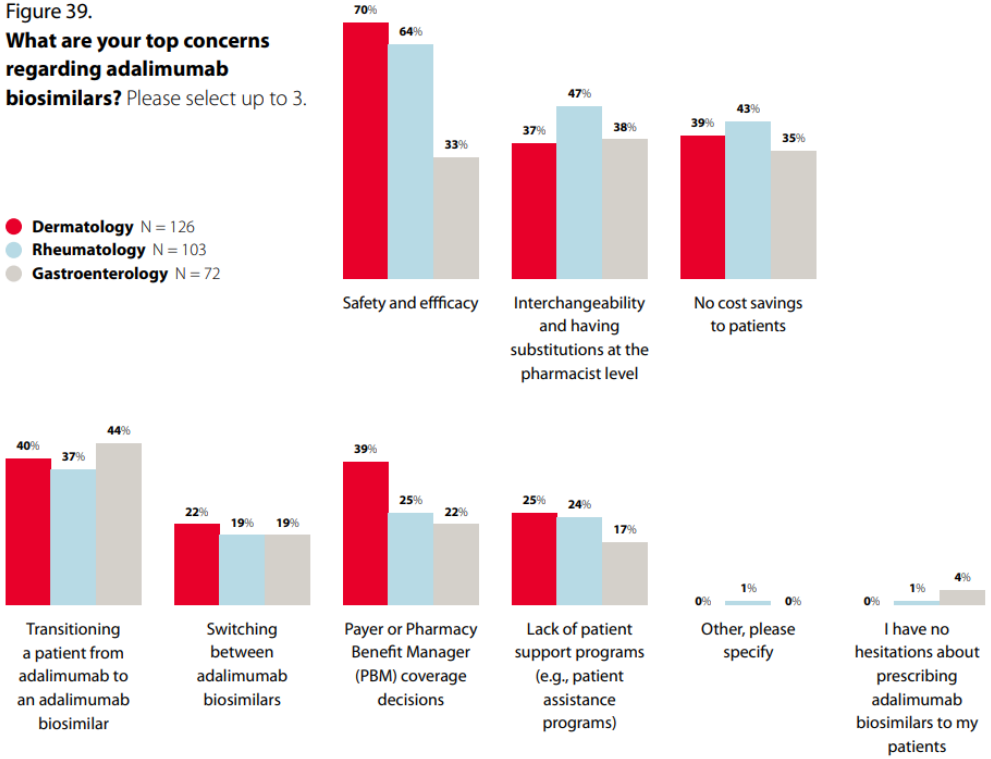
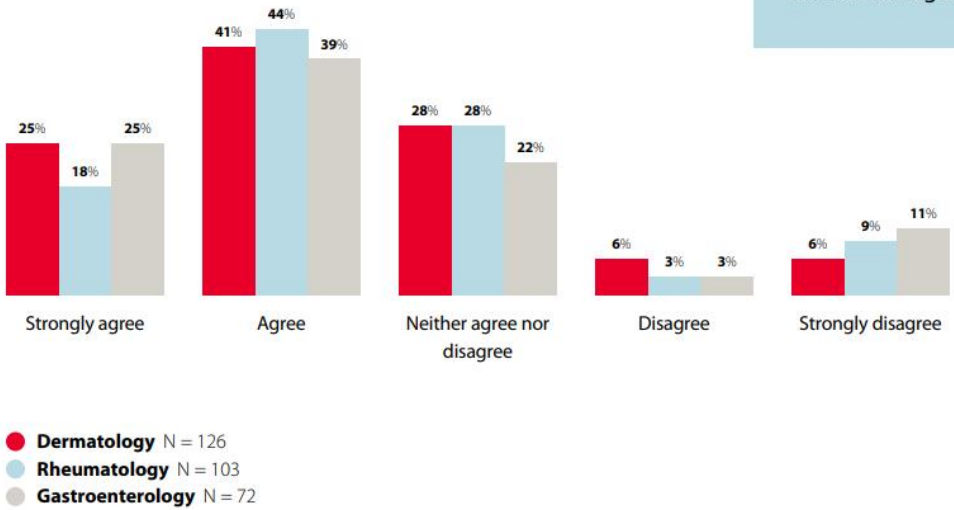


Figure 38.

To what extent do you agree with the following statement? I will only feel comfortable prescribing an adalimumab biosimilar if it has the interchangeability designation.

Over 60% of providers across all therapeutic areas will only feel comfortable prescribing an adalimumab biosimilar if it has an interchangeability designation



[Preview: 2023 Biosimilars Report (cardinalhealth.com)]

Product attributes most commonly cited as “very important”

Dermatologists

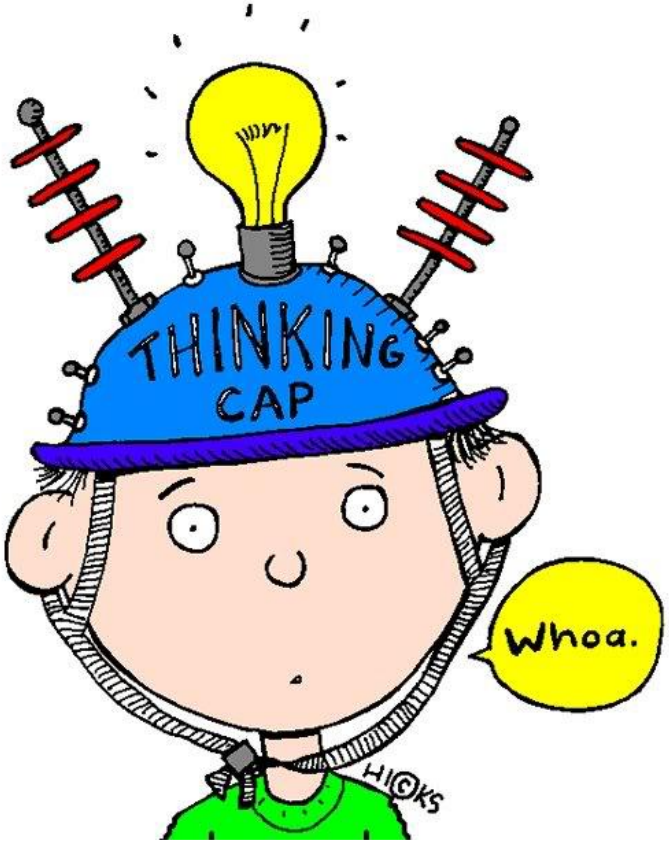
- Device/Ease of Use **(72%)**
- Interchangeability **(70%)**

Rheumatologists

- Citrate-Free **(62%)**
- Interchangeability **(60%)**

Gastroenterologists

- Device/Ease of Use **(69%)**
- Citrate-Free **(67%)**



How am I going to keep all this straight?

Approval Status	Product	Company	Estimated Launch	Seeking Interchangeability	Concentration	Citrate Free	Latex Free	Needle Size
FDA Approved	Amjevita™	Amgen	January 31, 2023	Yes	Low (50MG)	Yes	No	29G Syr. / 27G Pen
	Hadlima™	Organon	June 30, 2023	No	Low (50MG)[1]	No	Yes	29G Syr. / 29G Pen
	Cyltezo®	Boehringer Ingelheim	July 1, 2023	Yes (October 18, 2021)[2]	Low (50MG)	Yes	No	27G Syr. / 27G Pen
	Hulio™	Viatris	July 31, 2023	No	Low (50MG)	Yes	Yes	29G Syr. / 29G Pen
	Hyrimoz™	Sandoz	September 30, 2023	No	Low (50MG)	No	No	27G Syr. / 27G Pen
	Abrilada™	Pfizer	November 20, 2023	Yes[3]	Low (50MG)	Yes	Yes	29G Syr. / 29G Pen
Pending Approval	Idacio®	Fresenius Kabi	September 30, 2023	No	Low (50MG)	Unknown	Unknown	Unknown
	CHS – 1420	Coherus	December 15, 2023	No	Low (50MG)	Unknown	Unknown	Unknown
	AVT-02	Teva	TBD (Post Oct 2022)[4]	Yes	High (100MG)	Yes	Yes	Unknown
	CT – P17	Celltrion	TBD	No	High (100MG)	Yes	Yes	29G Syr. / 29G Pen
	ABP – 501 HC	Amgen	TBD	Yes[5]	High (100MG)	Yes	No	29G Syr. / 27G Pen

***Sources**: all information in this table is publicly available information*

[1]Samsung Bioepis conducted a Phase I clinical trial comparing two formulations of Hadlima™ (50MG and 100MG) (NCT04514796)

[2]Boehringer Ingelheim was granted interchangeability from FDA after positive results of a switching study between Cyltezo® and Humira® (Voltaire-X)

[3]Pfizer Phase III clinical trial to evaluate interchangeability between Abrilada™ and Humira® (NCT04230213)

[4]Alvotech and AbbVie are currently in litigation, but Alvotech has agreed that they will not launch "at-risk" prior to a court decision scheduled for Oct. 31, 2022

[5]Amgen Phase III clinical trial to evaluate multiple switches between a high-concentration formulation of Amjevita™ with Humira® (NCT05073315)

† https://www.fiercepharma.com/special-report/top-20-drugs-by-2020-sales-humira

Last updated: 1.5.2022

Summary

- Biosimilar agents go through extensive testing to ensure they are similar in nature to the reference biologic and prove no clinically meaningful difference
- New designation of interchangeability within the US biosimilar market
- Biosimilar uptake has been slow in the united states but gaining steam with the adalimumab biosimilars entering the landscape
- Biosimilar agents for use in rheumatology are currently available in the US for infliximab, rituximab, and now adalimumab


THATS THE END OF OUR PRESENTATION!
ANY QUESTIONS?
makeameme.org