Biosimilar Current Market analysis – 2019

Mayuri Mathuria

What are biosimilars and why we need to know about them?

Unlike Generics biosimilars are very complex molecules exceeding 1,50,000 daltons in size and are very sensitive to storage and handling conditions

Biosimilars have the potential to generate immune response unlike generics and each batch is slightly variable then the previous one

They require a huge investment(about 3 billion) for complex manufacturing processes and storage unlike generics which can be produced in a low budget(2- 3 million)

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What is trending in the biosimilars landscape…

Price erosion increased moderately in the US – biosimilar list price discounts over originators are >30%

- In the US: Pfizer's Nivestym (filgrastim biosimilar) and Retacrit (epoetin alpha biosimilar), Coherus' Udenyca (pegfilgrastim biosimilar), Mylan's Fulphila (pegfilgrastim biosimilar), all have launched at >30% WAC discount over their respective reference products – biosimilar ASP's (closest proxy to net price) are on average 40-50% lower than the originator's WAC
- In EU, for adalimumabs, price erosion is higher with list price discounts reaching 40% in several EU5 countries for biosimilars and the originator offering an 80% discount in Nordic nations

Companies positioning biosimilar portfolios as "one-stop shop" to build/ bolster brand presence

- Biosimilar companies have been positioning themselves as 'one-stop shops' for payers – e.g. Sandoz, Pfizer, Lilly, Sanofi
- Pfizer has developed six oncology biosimilars, three each in supportive and therapeutic oncology to further support its established brand presence in oncology

Biosimilar consolidation due to manufacturer collaborations and exits from later movers

- Biosimilar developers are re-assessing their launch strategies while evaluating the overall ROI – companies like Momenta, BI have reduced their biosimilar efforts likely after conducting a cost-benefit analysis

Due to expected launches and policy implementation, 2019 will be eventful for biosimilars

- The US and EU could see entry of 14 and 10 biosimilars respectively in 2019
- In the US, expected clarity around issues such as interchangeability, CMS reimbursement in part B and part D

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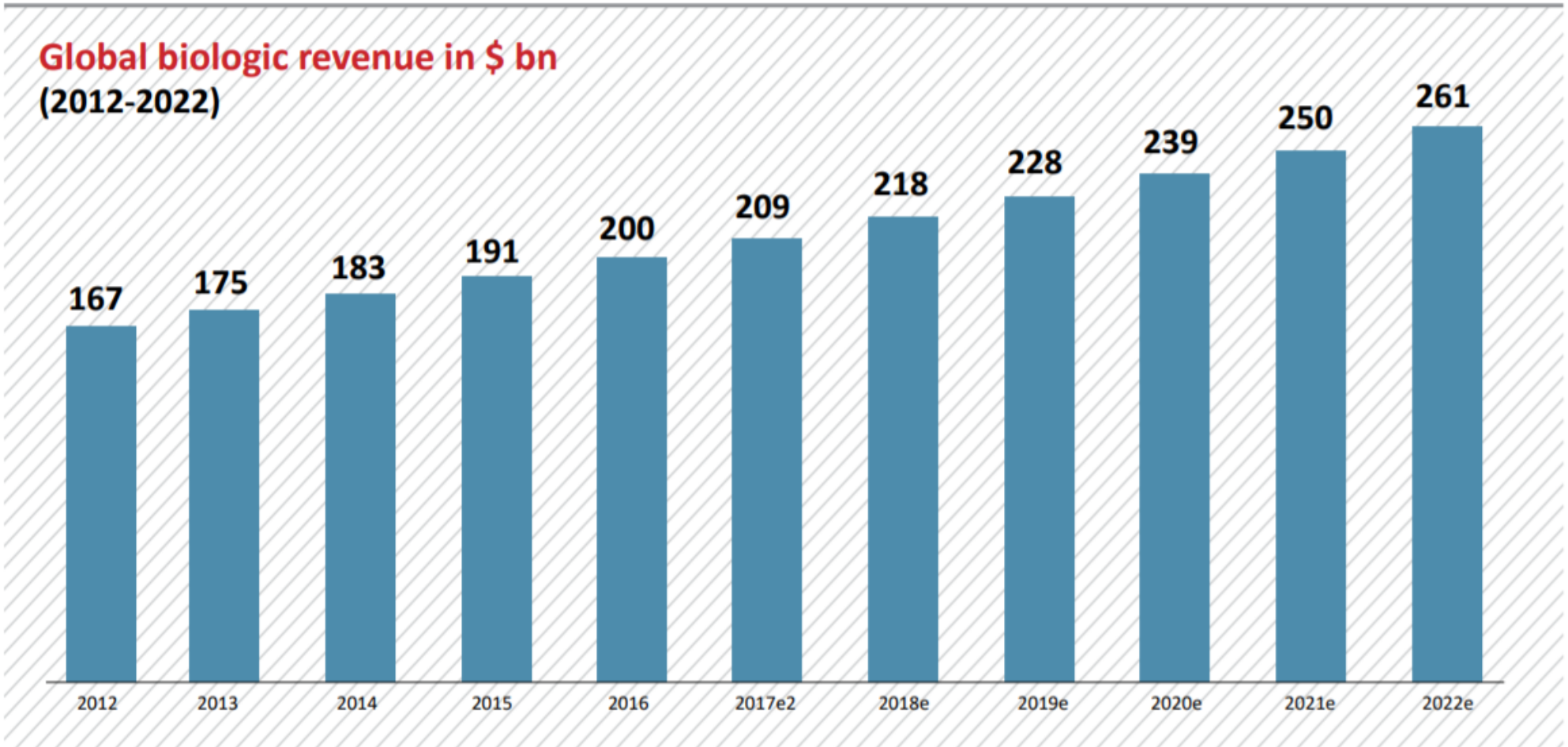
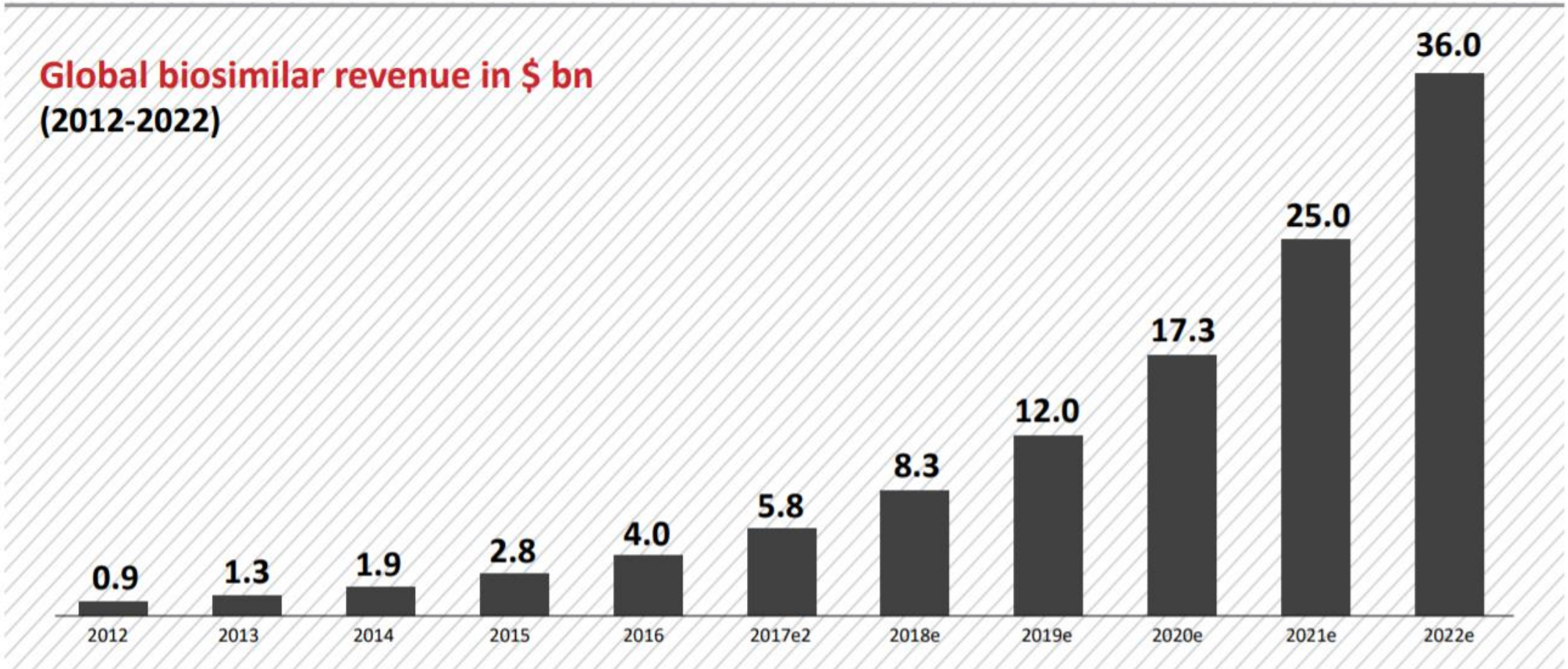
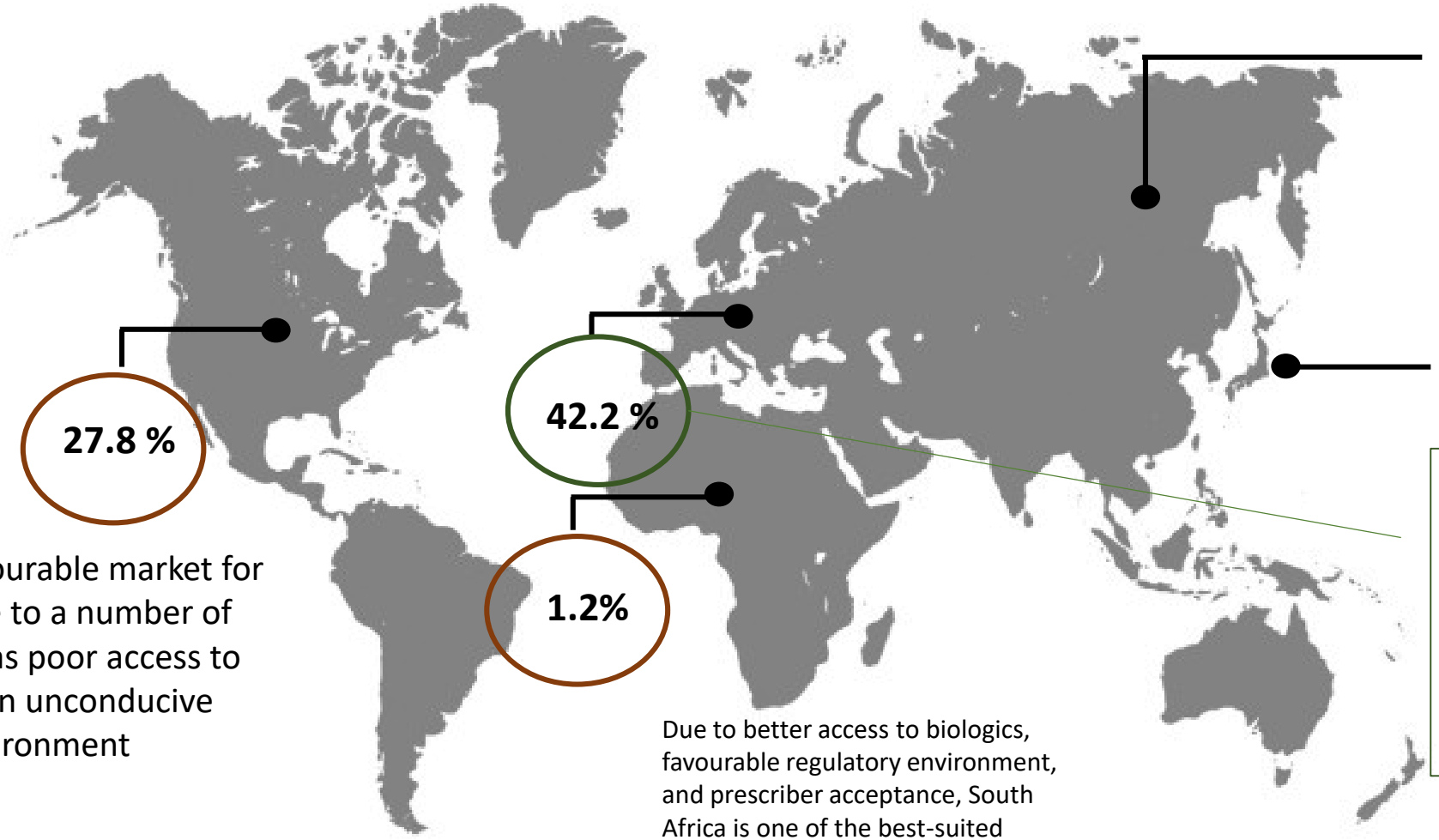
Biosimilar Market Landscape Analysis

By 2022, the global biosimilar market is expected to reach USD 36 billion, while the biologic market is expected to reach USD 261 billion.




Global biosimilar revenue in $ bn
(2012-2022)
0.9
1.3
1.9
2.8
4.0
5.8
8.3
12.0
17.3
25.0
36.0
2012
2013
2014
2015
2016
2017e2
2018e
2019e
2020e
2021e
2022e

With a near share of 85% US, Japan and Europe are the major contributors to the global biologic and biosimilar sales



US is not a favourable market for biosimilars due to a number of reasons, such as poor access to biologics and an unconducive regulatory environment

Due to better access to biologics, favourable regulatory environment, and prescriber acceptance, South Africa is one of the best-suited market for biosimilars.

Europe and Brazil are better markets for biosimilars because of their favourable regulatory environment and payer access and assessment

Amgen's Neulasta has started to witness competition from biosimilars globally

Amgen plans to combat Humira biosimilars with value differentiation and expansion of patient support services

	US	EUROPE	CANADA
Mylan / Fulphila (pegfilgrastim-jmdb) injection	Community Oncology and Hospital-based Outpatient Clinics Included in United HealthCare's Medicare Advantage Plan India · Syringe a passive needle guard & a plunger with a larger head · 33%	*Approved*	▪ Pre-registration
Coherus / NOW FDA APPROVED UDENYCA pegfilgrastim-cbqv	340 b and GPO's (non 340 B and independent clinics) US · Syringe with an automatic needle safety guard · 33%	*Approved*	• *No Development*
mundipharma / PELMEG	▪ *No development*	To engage with EU and national authorities, focus on payers, hospitals and local presence Europe · 27%	▪ *No Development*
SANDOZ / ZIEXTENZO	• *No development*	Experience of successfully marketing filgrastim biosimilar Zarzio in Europe with its subsidiary Hexal Austria and Slovenia · 27%	No Development
Apobiologix / LAPELGA	▪ *No development*	▪ *No development*	Focusing on lobbying with Health Canada to gain a preferential reimbursement for its pegfilgrastim biosimilar Canada · 25%

How is AMGEN protecting its blockbuster drug?

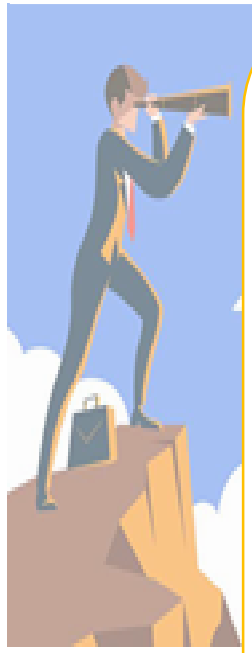
- Growing Neulasta units through increased cycle penetration, particularly in breast cancer and NHL patients
- Investment in Direct-to-Patient programs
- Differentiation of the Amgen franchise
- Differentiating Neulasta from short-acting competition

Sources :1. Seeking Alpha; 2. Coherus; 3. Seekingalpha; 4. CoherusComplete; 5. Centerforbiosimilars; 6. Novartis Oncology; 7.Businesswire Sandoz; .

The European adalimumab market continues to heat up with the entry of multiple adalimumab biosimilars – lucrativeness of the market likely outshines the ever-growing competition

Humira (adalimumab) biosimilar market in Europe

Key trends in EU Adalimumab market



- As per analyst Bernstein Gal, 50% adoption of Humira biosimilars by volume is expected within the first year of its launch
- AbbVie is expecting Humira biosimilars to erode European sales by about 40%
- In England, Amgevita's improved formulation has helped it to gain an additional market share thus proving that physician's opinion is dependent on patient's convenience and can override economic incentives
- Switches are not unidirectional(biologic to biosimilar) - In Germany where Humira's improved formulation has been the reason for shift from Imraldi back to Humira.
- Due to intensive crowding biosimilar companies like BI are trying to focus on other research areas

Biosimilars in Adalimumab market are facing huge discount challenges from the originator and need new strategies to sustain longer

How is Abbvie planning to retain its Humira market?

Up to 89% discount in to chase away biosimilar competitors out of the market

New products like upadacitinib and risankizumab in the immunology space

Losses due to biosimilars to be covered by non Humira sales - more than $35 billion by 2025

Humira biosimilars are experiencing slow uptake than anticipated potentially due to competitive discounting from AbbVie

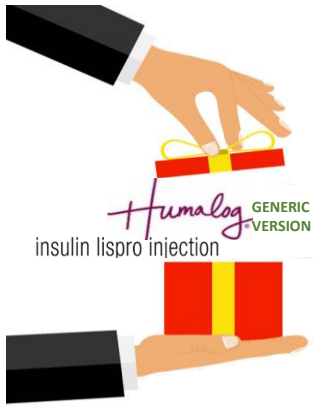
93%	27%	19%
15%	10%	3%

Denmark with its winner- takes all tender has switched more than 80%of its patients to Humira biosimilars while Germany is showing a faster acceptance than UK

Sources : Journals.plos; 2.Gabionline; 3. Gabi-journal; 4. Centerforbiosimilars; 5. Abbvie;

Authorized versions of branded biologics

Eli Lilly to launch a lower-priced version of Humalog



~~$274.7~~ **$137.35** Per vial

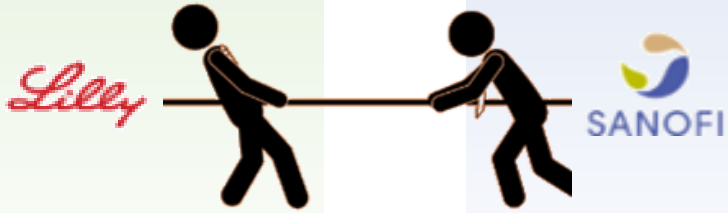
Segments targeted will include patients without any insurance coverage

- Available as an authorized generic through a Lilly subsidiary, **ImClone Systems**

Sanofi revamps its Insulin's VALyou Savings program

~~$99~~ **$9.9** Per vial

All patients regardless of income and insurance coverage



Sources : 1. Lilly; 2. Sanofi; 3. Centerforbiosimilars; 4. Patientsforaffordabledrugs

Celltrion, a formidable biosimilar player, plans to increase its presence with a 'twin-track' strategy for infliximab biosimilars

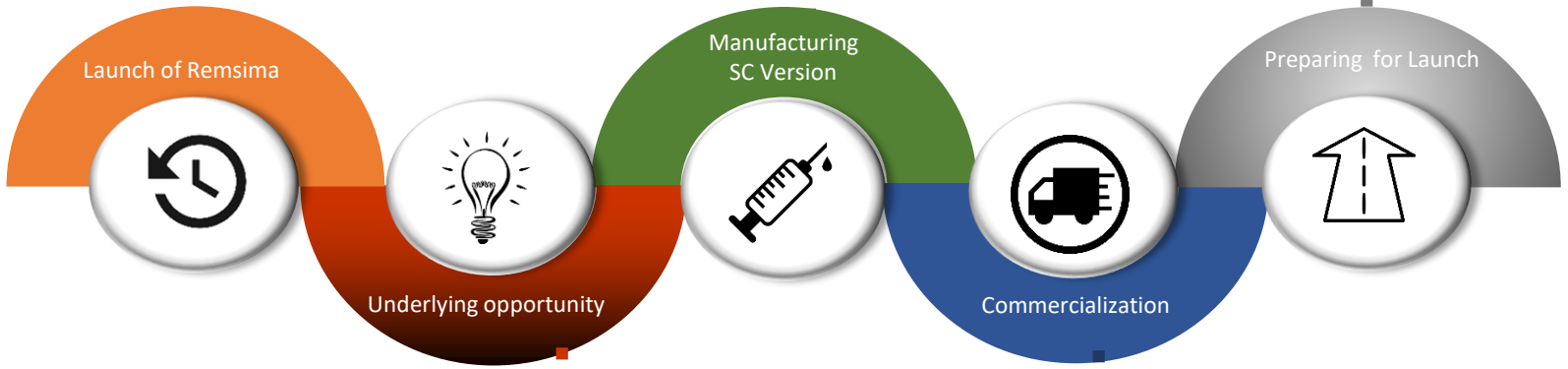
Celltrion to try hands on direct commercialization for Remsima SC

Clinical Trials and Device Manufacturing

- US FDA allowed Celltrion to conduct only Phase III stage clinical trials for Remsima SC
- Committed $51 million to its site in Cheongju, South Korea for Remsima SC
- The launch for the device is expected till early 2020

Future Plans

- Plans to use diversifying products as a promotion strategy for both Remsima and Remsima SC
- The SC version is patent protected till 2037 and is registered in 90 Countries.



Remsima
Infliksimab

Remsima launch 2017

- With the help of 22 distributors Remsima catered the need of patients when naive

Celltrion had a potential demand base to target

- Later realized the opportunity associated with newer SC version that even originator failed to possess
- Also decided to do away with commercializing via other partners and took sole charge for the same

Plans for Direct commercialization

- Directly through 'Celltrion Healthcare', unlike its current distribution strategy through local partners

"Establishing its own sales network would allow Celltrion to gain an edge in pricing and enable it to directly handle every process" - Seo, Chairman of Celltrion

Sources : 1 Pharmaphorum; 2. Businessdaily; 3. Centerforbiosimilars; 4. Theinvestor; 5. Bioprocessinternational; 7. BioPharma;

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Early mover exploring market - synergistic and cost effective manufacturing and commercialization seems to be the key for competitive market as many companies are exiting the market

Few players find relevant opportunity in investing in biosimilars sector

Enhanced investment

HEALTHCARE CELLTRION

Planning to set up EU sales unit

Biogen

Increased stake in Samsung Bioepis from 5% to ~50%

Collaboration and acquisition

Mylan®

Entered into other collaborations for biosimilars despite Biocon

mundipharma

Acquired Cinfa's biosimilar business

Few others are retracting from biosimilar investment

Business restructuring

Pfizer STOP **5 biosimilars**

Change in Focus

MOMENTA STOP **5 biosimilars** to focus on **Rare Disease portfolio**

Continue ▶ **adalimumab biosimilar and aflibercept biosimilar (late stage)**

Failure in addressing regulatory questions

SANDOZ STOP **adalimumab biosimilar** post receiving **CRL** from the **FDA**

Market challenges

Merck KGaA terminated its contract with SAMSUNG BIOEPIS

Sources : 1. Centerforbiosimilar ; 2. Pharmajapan ; 3. Bioprocessinternational ; 4. Gabionline

Many companies are investing in fueling up their manufacturing sites for efficient production

Pharma companies worldwide are trying to build up their biosimilar reputation with efficient manufacturing and distribution

- To establish a production site in Cheongju, South Korea
- The investment is to cover up for lack of space availability and workforce at the older Incheon Songdo site which is run by Celltrion
- An investment of a 3rd 120,000 L biologics plant at the Songdo plant is in line with the companies' plans to expand

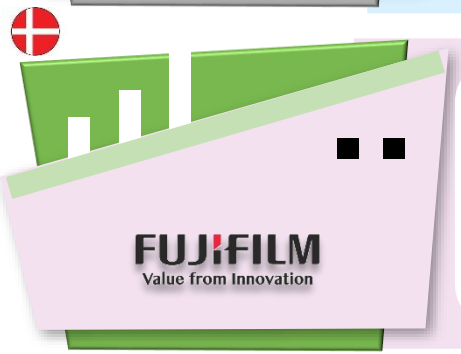
$ 51 million

Remsima SC

- Purchased manufacturing site in Raleigh, North Carolina, from Xellia Pharmaceuticals
- It is the first US plant for the company who previously relied on contractors to produce the sterile injectables
- The terms of the deal were not fully disclosed

FDA Approved

Lyophilized formulations of biosimilars



- Acquired Manufacturing site ApS in Hillerød, Denmark from Biogen
- The site has 90,000 L production facility with assembly, labelling and packing capabilities, quality control laboratories and warehouses
- The existing workforce of approx. 800 employees, will continue employment under Fujifilm.

$ 890 million

Tysabri and third party products

Sources : Coherus Seekingalpha CoherusComplete Centerforbiosimilars Novartis Oncology Businesswire Sandoz

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Germany continues to formulate policies in favor of biosimilar developers

Germany shows a positive attitude for biosimilars with companies providing discounts from 10-40%

1st DRAFT

The first draft of GSAV introduced:
- marketing authorizations under conditional approval for drugs
- encouraged biosimilar use
- additional monitoring and drug recall power to higher authorities

2nd DRAFT

Pharmacy-level biosimilar substitution permissible only after the G-BA has issued guidelines
- To occur by mid 2022, after a lead time of three years
- Until then, physicians will be responsible for switching patients from originator to biosimilars

Biosimilar uptake targets will be defined at the regional level

IMPLICATION

Law still subjected to the Federal Council's approval and is expected to be implemented by mid 2019
- If implemented, this could further aggravate erosion of Humira in Germany
  - Samsung Bioepis' adalimumab biosimilar, Imraldi has already gained 62% of the German adalimumab market, per a recent report

Various steps enforced by the German regulatory bodies to push biosimilars forward in the market

- Physicians who achieve set biosimilar quotas are allowed to bill additional services for their patients
- Biosimilars included in the reference pricing system alongside the originator drug
- Physician-led switching is encouraged for patients who have already been treated with a reference biologic
- Tendering is available at hospital, regional and national levels; tenders operate in outpatient setting and are managed by the SHI

Sources : 1. Eucope.org ;2. Mapbiopharma ; 3. GaBi

US continue to formulate policies for biosimilars

The regulatory landscape has a lot of proposals waiting in line to change the course of wave for biosimilars

Naming guidelines

- FDA has decided to designate a proper name for all interchangeable biosimilar drugs, merging the product's core name with a specialized lower-case, four-letter suffix "devoid of meaning
- This requirement has also been maintained for already approved or newly licensed biosimilars and newly approved biologics

Punishing unethical tactics against biosimilars

- The drugs under investigation include are AbbVie's Humira; Amgen's Enbrel; and Sanofi's insulin glargine, Lantus
- Biologics use various tactics such as exclusive contracts with PBMs and insurers and their financial backing of an industry trade group, non-profit alliances like for Safe and Biologic Medicine - the Biotechnology Innovation Organization (BIO), that spends over $10M each year lobbying Congress

BIO AMGEN Genentech A Member of the Roche Group

Prime members" of the nonprofit Alliance for **Safe and Biologic Medicines**, a network of industry-funded groups aimed at curbing the spread of biosimilars

Trump's 2020 report

Reduction of Payment Rate

For single-source biosimilars from 106% to 103% of WAC to reduce excessive payments

PROPOSAL

Removal of Pass through

Remove transitional pass-through payment for biosimilars from Medicare Outpatient Prospective Payment System

PROPOSAL

Reduce cost sharing to $0

For generics, biosimilars & multiple source drugs among LIS beneficiaries to encourage the use of higher value products.

PROPOSAL

Amending PHSA*

Biosimilars do not have to meet separate standards(strength, labelling, packaging, quality) unlike other non biologics.

PROPOSAL

180 day forfeiture provision

Applicant can avoid 180 day forfeiture only when there is a change in the requirements for approval

PROPOSAL

Sources : 1. Managedhealthcare; 2. Seekingalpha; 3. Centerforbiosimilars; 4.Centerforbiosimilars

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There is a shifting disease profile to chronic conditions from infectious diseases which can be better treated by large molecule therapies

Patients cannot afford and do not have access to high priced biologics

Government now a days are pushing development of their domestic pharmaceutical industries

Physicians are the key influencers and deciders of patient therapy and often make prescription decisions for biosimilars based on perceived ability to pay

KEY DRIVERS FOR BIOSIMILARS IN US and EUROPE

Regulatory Uncertainty

- The administrative strategies administering biosimilars are still in transition, with real markets like China and US lacking steady and clear pathways

Production Complexity

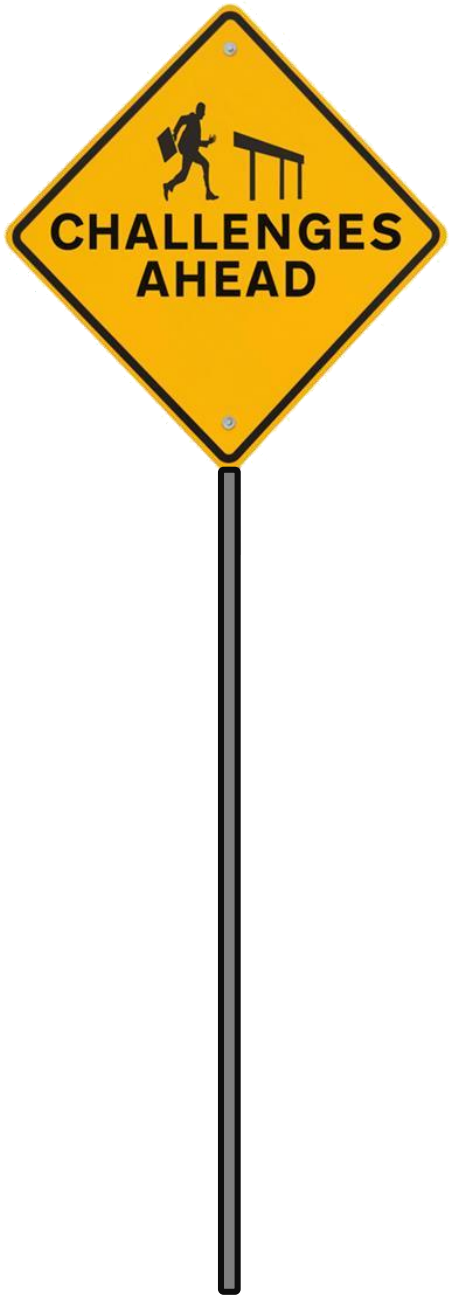
- Biosimilars are increasingly mind boggling to create because of the intrinsic fluctuation between one living cell and another, and the failure to precisely recreate the assembling or structure of the originator biologic.

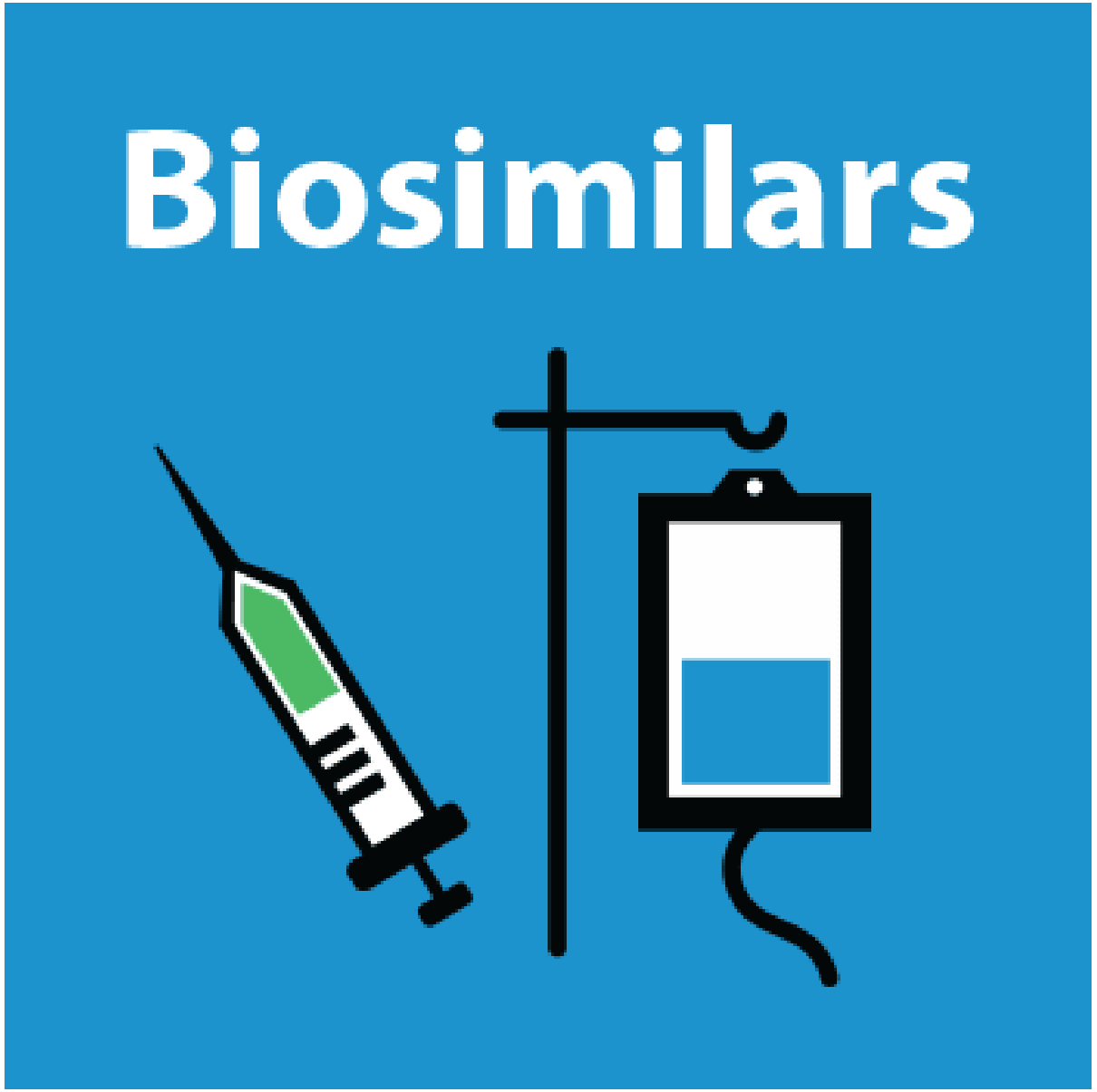
Interchangeability

- The absence of clear rules on substitutability and interchangeability with reference biologics will probably make doctors practice more alert in recommending biosimilars until they gain comfort with the quality and viability of biosimilars.

Competition

- Biosimilars face competition from two sources: biobetters from marked organizations and lack of brand awareness from purchasers





“A bridge between *affordability* and *accessibility* of Health care”