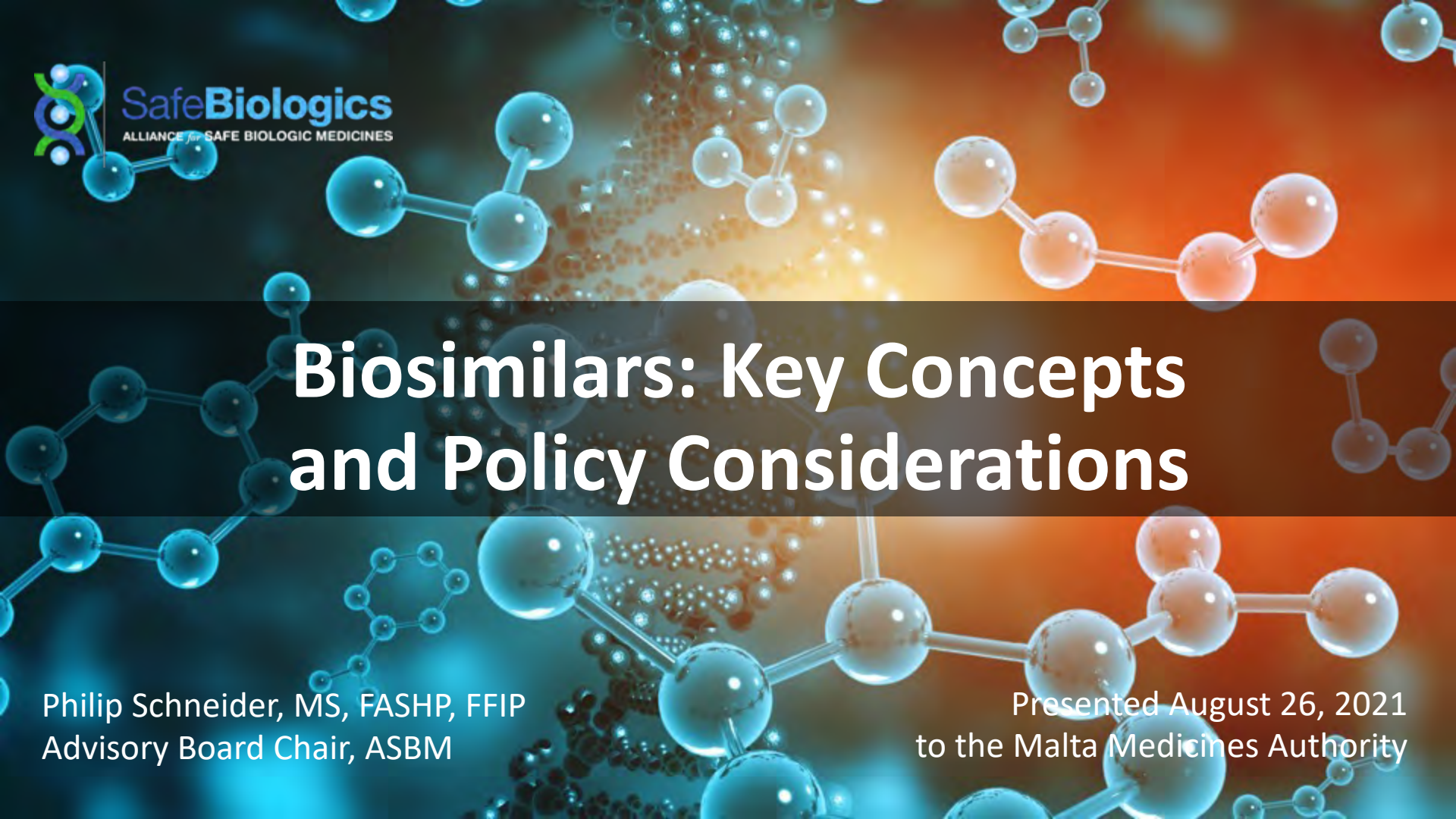


Biosimilars: Key Concepts and Policy Considerations

Philip Schneider, MS, FASHP, FFIP
Advisory Board Chair, ASBM

Presented August 26, 2021
to the Malta Medicines Authority

Introduction

- **Philip Schneider, MS, FASHP, FFIP**
- Advisory Board Chair, Alliance for Safe Biologic Medicines
- Past Vice President, International Pharmaceutical Federation (FIP)
- Past-President, American Society of Health-system Pharmacists
- Professor of Pharmacy, Ohio State University

About ASBM

SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

Formed in 2010 with the passage of the Affordable Care Act (ACA) and Biosimilar Price Competition and Innovation Act (BPCIA); with the goal of keeping patient safety at the forefront of biosimilar policy discussions.

ASBM's Steering Committee is composed entirely of patient and physician member organizations.

- PATIENT ADVOCATES
- PHYSICIANS
- PHARMACISTS
- RESEARCHERS
- MANUFACTURERS (INNOVATOR & BIOSIMILAR)

LYMPHOMA COALITION
Worldwide Network of Lymphoma Patient Groups

American Gastroenterological Association

CSRO
Coalition of State Rheumatology Organizations

More than 130 organizations spread across six continents; the More than 130 organizations spread across six continents; the majority of these are patient groups, including several patient coalitions.

ASBM Physician and Pharmacist Surveys

U.S. Physicians
2012: n=376
2015 n=400
2015: n=400
2019: n=202
2021 n= 400 (in progress)

U.S. Pharmacists
2015 n=401

Latin American Physicians
(Argentina, Brazil, Colombia, Mexico)
2015: n=399

Canadian Physicians
2014: n=427
2017: n=427
2021 (planned)

European Physicians
(France, Italy, Germany, Spain, Switzerland, UK)
2013: n=470
2019: n=579

Australian Physicians
2016: n=160

All surveys available at www.SafeBiologics.org/surveys

Sharing Perspectives With Regulators

SafeBiologics
ALLIANCE for SAFE BIOLOGIC MEDICINES

WORLD HEALTH ORGANIZATION INN CONSULTATIONS
(2013-2021)

AUSTRALIAN DEPARTMENT OF HEALTH, THERAPEUTIC GOODS ADMINISTRATION (2017)

HEALTH CANADA, CANADIAN HEALTH MINISTRY (2017)

INTERNATIONAL CONFERENCE OF DRUG REGULATORY AUTHORITIES (ICDRA) (2016, 2018)

ASBM INTERNATIONAL REGULATOR FORUMS ON NOMENCLATURE HARMONIZATION
(FDA, HEALTH CANADA, WHO) 2018-2019

EU COMMISSION/EMA BIOSIMILARS MEETING (2019)

U.S. FDA/FEDERAL TRADE COMMISSION WORKSHOP ON BIOSIMILAR COMPETITION
(MARCH 2020)

Presentation Overview

I. General Concepts

II. Nomenclature and the Importance of Non-Proprietary Names

III. Prescribing and Switching

IV. Economic Considerations/Pricing

V. Future of Biosimilar Market/Long-Term Sustainability

I. General Concepts

What is a Biologic Medicine?

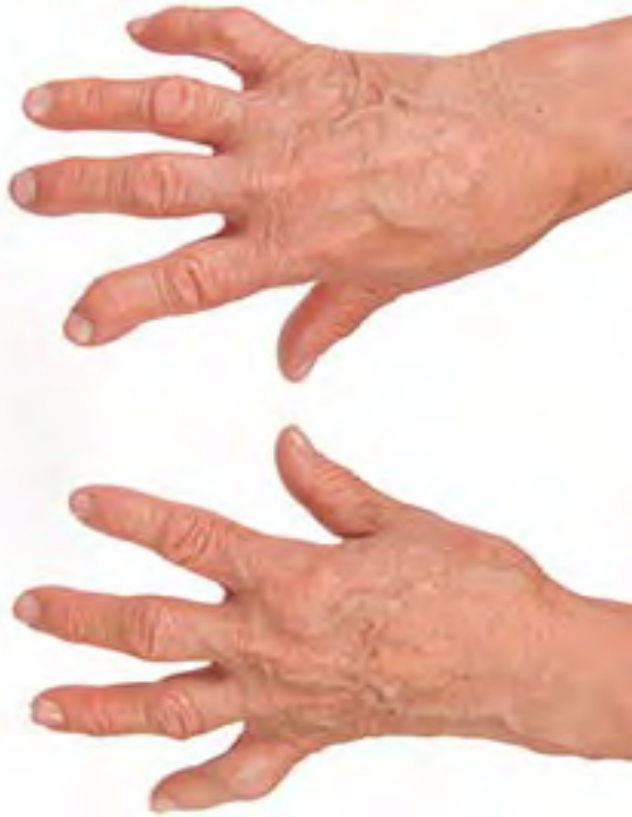
- A **biologic medicine** is a **substance** that is made **from** a **living organism** or its products and is used in the prevention, diagnosis, treatment, or cure of a disease. Biologic medicines include:
  - antibodies
  - vaccines
  - interleukins (these can regulate immune responses)
- At a molecular level, biologic medicines are often 200–1000 times the size of a chemical drug molecule and are far more complex structurally. They are highly sensitive to handling and their environment.
- Biologics are more difficult to characterize and manufacture than chemical drugs.
- Due to their size and sensitivity, biologic medicines are almost always injected into a patient's body.

Benefits of Biologic Medicines

- Biologic medicines have made a significant difference in the lives of patients with serious illnesses, including cancer, blood conditions, auto-immune disorders such as rheumatoid arthritis (RA) and psoriasis, and neurological disorders like multiple sclerosis (MS).
- By understanding the mechanisms of diseases, companies have developed biologic medicines to target and modify the underlying causes of disease, potentially altering the course of the disease rather than simply treating symptoms.
- The development of new biologic medicines may be the best hope for effectively treating diseases for which there are currently no cures.

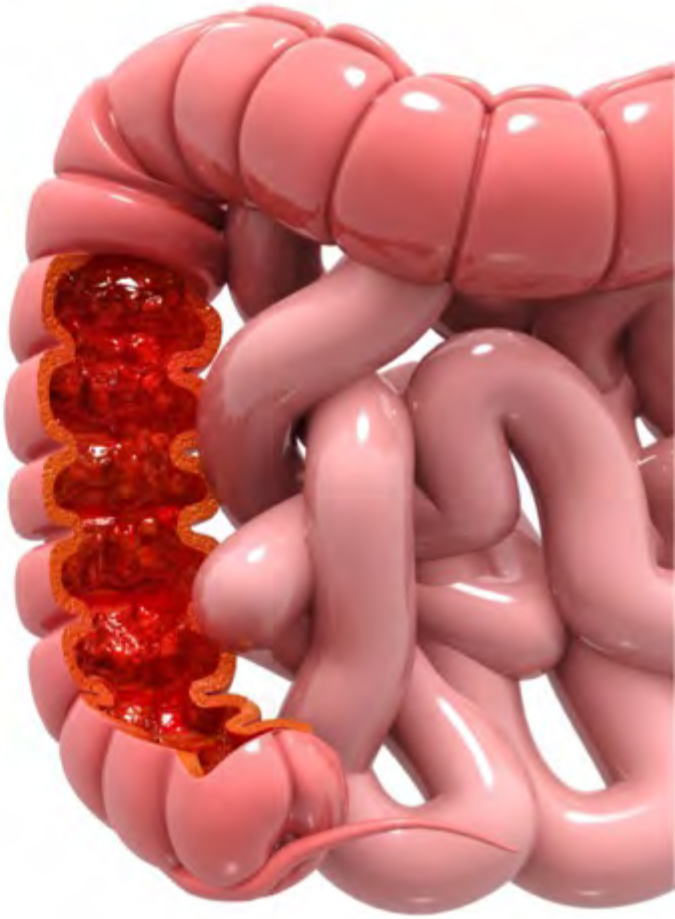
Example: Rheumatoid Arthritis

- Advances in the understanding of RA over the last 20 years have led to a new treatment paradigm, where reducing disability and achieving remission are now possible goals.
- Once researchers understood the underlying inflammatory mechanisms of RA, scientists developed disease-modifying biologic medicines to target the proteins that regulate inflammation. Biologic medicines have proved effective in slowing down disease progression and joint damage, helping to improve daily function.



Example: Colorectal Cancer

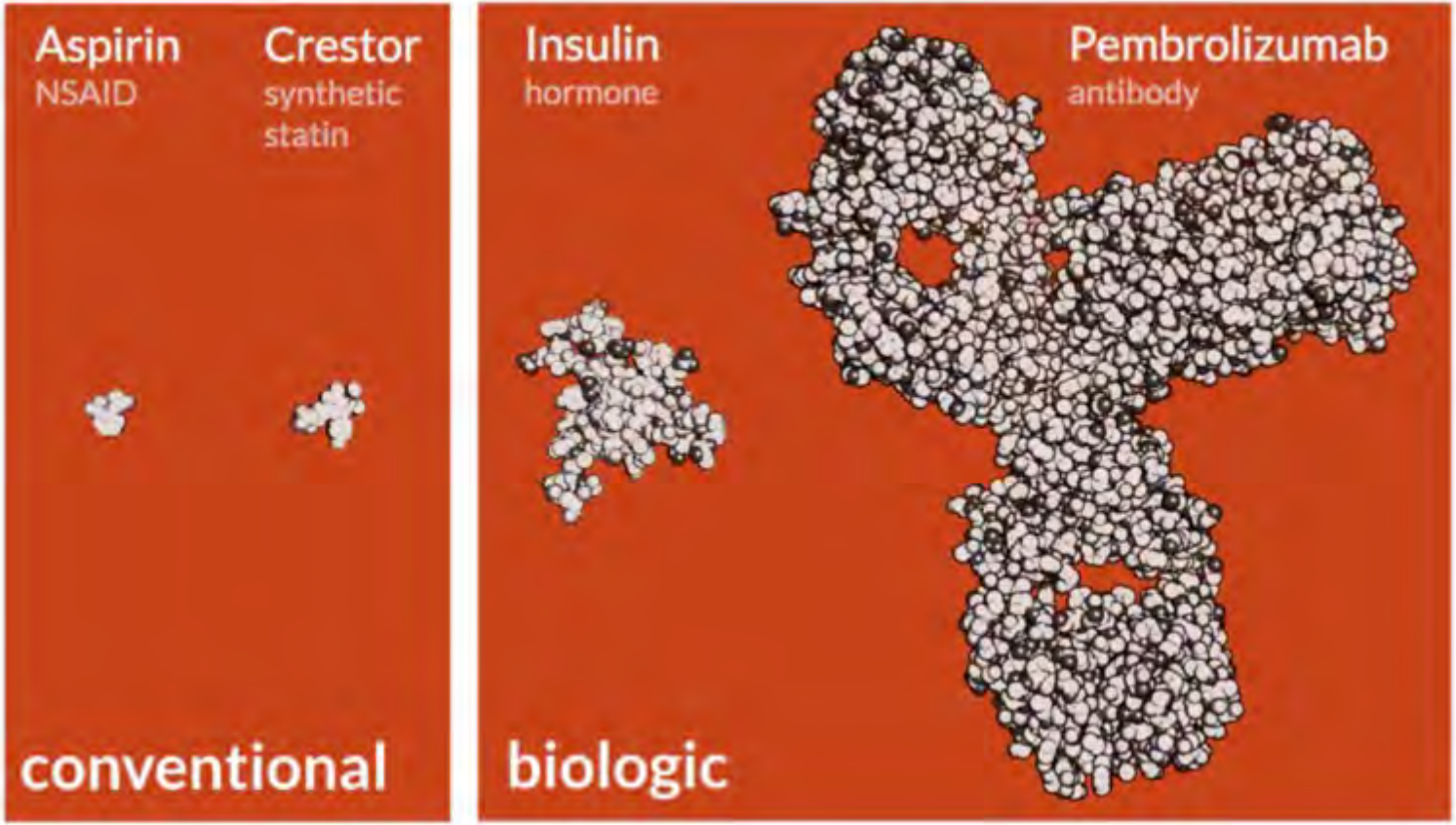
- Investigating cancer pathways and determining the molecular basis of cancer has led to the development of new targeted diagnostics and treatments. Traditionally, cancer has been treated with surgery, radiation, and chemotherapy. Biotechnology has contributed to significant advances in cancer treatment, including hormone therapies, biologics, and targeted therapies such as monoclonal antibodies.
- Some kinds of colorectal cancer are caused by the overexpression of epidermal growth factor receptors (EGFR), causing the overly rapid cell growth associated with most cancers. There are several EGFR inhibitors available to patients.

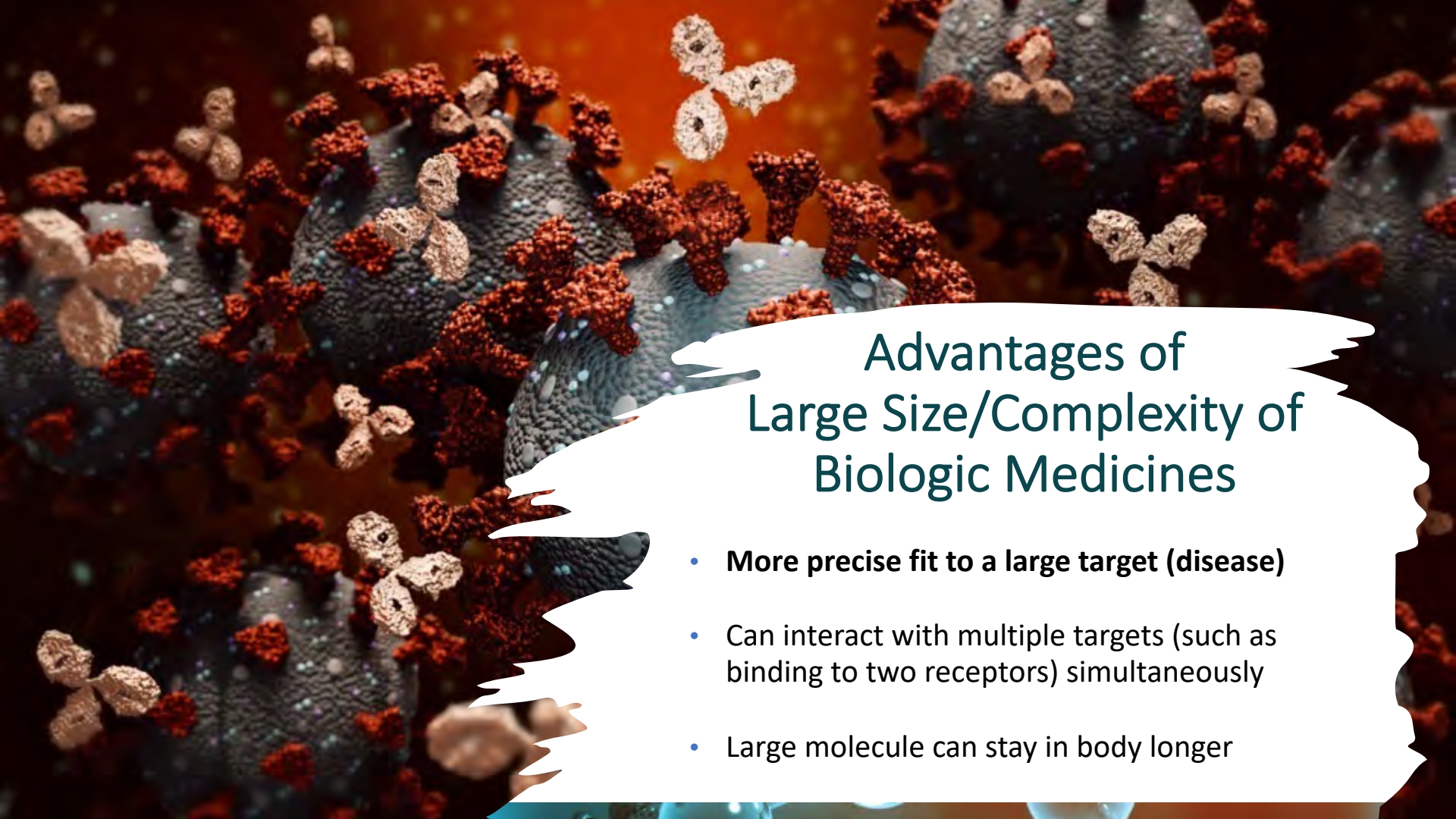


Size and Complexity of Biologics

"Biologics [and biosimilars] are like the Empire State Building, compared to a regular drug, which is like a small house"

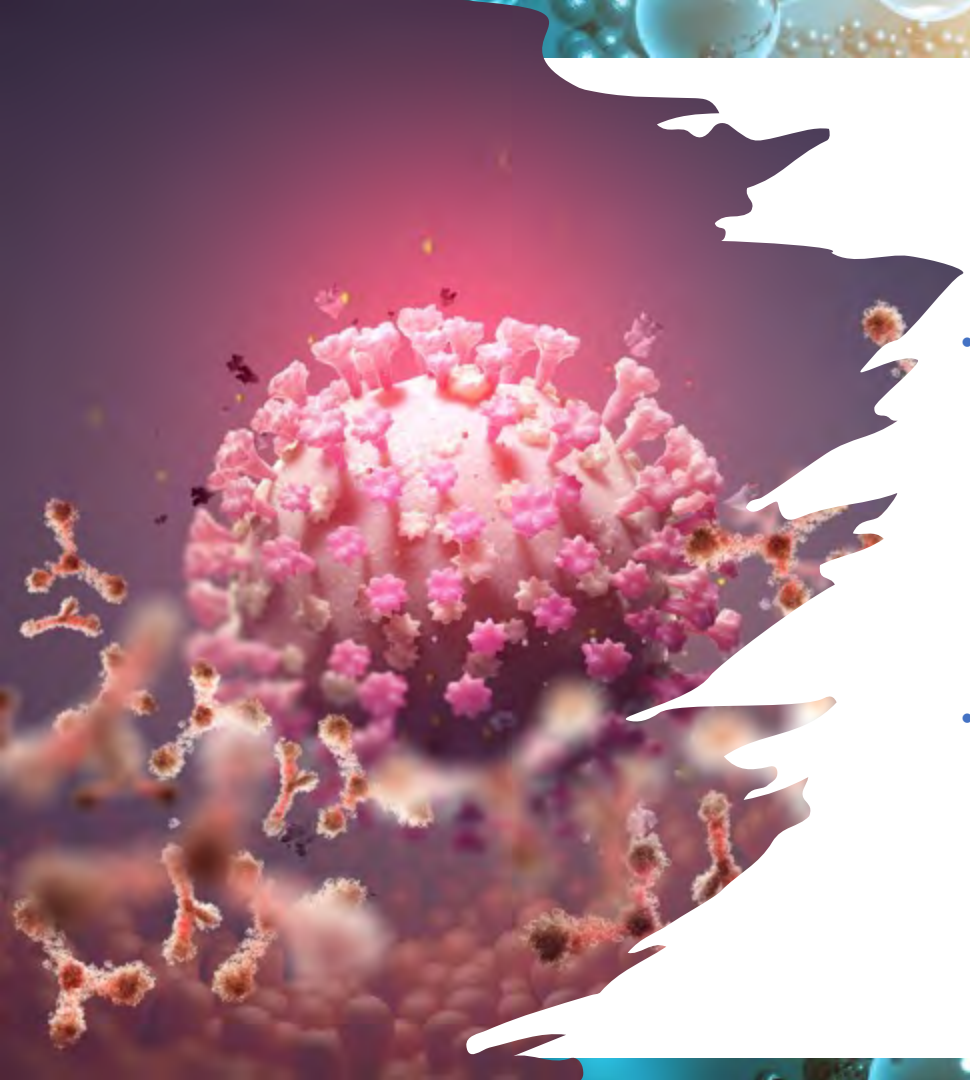
-Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research (CDER), FDA February 4, 2016


Aspirin
NSAID
Crestor
synthetic
statin
conventional
Insulin
hormone
Pembrolizumab
antibody
biologic



Advantages of Large Size/Complexity of Biologic Medicines

- **More precise fit to a large target (disease)**
- Can interact with multiple targets (such as binding to two receptors) simultaneously
- Large molecule can stay in body longer



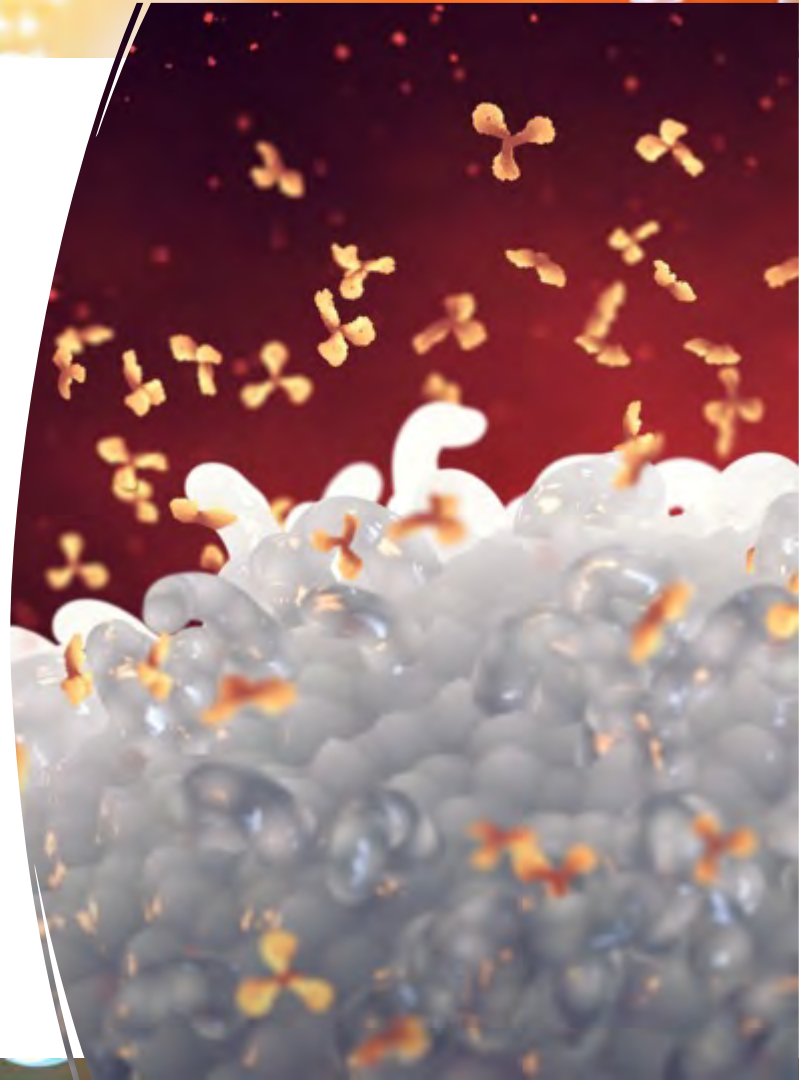
One Disadvantage of Large Size/Complexity: Immunogenicity

- **Biologics have provided new options in the prevention and treatment of diseases in which previous therapies treated only the symptoms.** However, because of their complexity, biologics are associated with additional risks. The most important of these risks is **the potential to cause immunogenicity.**

- Immunogenicity occurs when the immune system in the human body mounts an attack when a foreign substance enters the body. For example, when we catch a common cold (i.e. rhinovirus) or the flu (i.e., influenza virus), **our body responds by attacking these viruses, thereby neutralizing them.**

Potential for Immunogenicity is a Major Concern

- All biologic medicines are fairly large molecules and have the potential to induce unwanted antibody responses (i.e., be immunogenic).
- The unwanted immune response may be of no consequence for a patient or of serious consequence.
- Immunogenicity may neutralize the medicine, minimizing or eliminating the intended effect of the medicine.
- One of the main concerns is that the immune system may attack the endogenous protein, making the patient's condition worse than before the medicine was introduced.



What is a Biosimilar?

- Developing a biosimilar requires reverse-engineering an innovator biologic. **Biosimilars are often mistakenly referred to as “generic” biologics.**
- Unlike with generic copies of chemical medicines, the fact that they are made using living cells means biologic medicines **cannot be copied exactly. It can only ever be “similar” to its reference biologic.**
- Cost savings vary from 15%-60% over reference product depending on country.
- In January 2017, FDA issued draft guidance on how similar a biosimilar must be to earn a designation of **“interchangeable”**, meaning that the biosimilar has the **same clinical effects in a patient without additional risks.**
- **The U.S. approved the first interchangeable insulin product in July 2021.**

Why is Increasing Biosimilar Uptake Important?

Potential Savings to U.S. Market: Cigna/Evernorth Estimate

- Biologic drugs now represent ~2% of prescriptions, but ~43% of pharmacy spending in 2019. ($211 billion)
- Cigna subsidiary Evernorth expects growing biosimilar competition **<u>to save $225 - $375 billion in pharmacy</u>** spending by 2031.
- We will discuss economic and financial considerations in more detail later today.

1 https://www.evernorth.com/articles/the-coming-wave-of-biosimilar-medications

Europe Leads in Biosimilar Approvals

In the European Union (EU), a legal framework for approving biosimilars was established in 2003. This framework means that biosimilars can only be approved centrally via the European Medicines Agency (EMA) and not nationally.

EMA first developed guidelines for the approval of biosimilars via an abbreviated registration process during 2005 to 2006.

Omnitrope (somatropin) was the first product approved in the EU as a biosimilar in 2006.

To date, EMA has recommended the approval of 46 biosimilars (under 77 different marketing authorizations) within the product classes of:

- human growth hormone
- granulocyte colony-stimulating factor
- erythropoiesis stimulating agent
- Insulin
- follicle-stimulating hormone (FSH)
- parathyroid hormone
- tumour necrosis factor (TNF)-inhibitor
- monoclonal antibodies

http://gabionline.net/Biosimilars/General/Biosimilars-approved-in-Europe accessed 5/15/21

U.S. Biosimilar Approvals

- The U.S. adopted it biosimilar approval pathway in 2009 and FDA approved its first biosimilars in March 2015.

- As of approximately 10 years after implementation of the biosimilar approval pathway, **29 biosimilars have been approved by FDA, with 19 of those approvals granted in the last 2 years.** (For comparison, in the 10-year period following the creation of Europe's biosimilar pathway, EMA approved only 13 biosimilar products.)

- **Note:** 11 of the 46 products approved as biosimilars in Europe are approved in the US as "follow on biologicals" via the earlier, 505(b)(2) pathway (e.g. somatropin, insulin, teriparatide.)

https://www.fda.gov/drugs/biosimilars/biosimilar-product-information accessed 8/28/18

Canadian Biosimilar Approvals

- In Canada, the regulatory body for the approval of biologicals is the **Biologics and Genetic Therapies Directorate (BGTD) of Health Canada.**

- In March 2010, Health Canada finalized guidelines for biosimilars, which were previously called **subsequent entry biologics** in Canada
- The first biosimilar to receive approval in Canada was Sandoz's growth hormone treatment Omnitrope in 2009.
- To date, Health Canada has approved **34 biosimilars** within the product classes of human growth hormone, granulocyte colony-stimulating factor (G-CSF), insulin, monoclonal antibodies and tumour necrosis factor (TNF)-inhibitor.

http://www.gabionline.net/Biosimilars/General/Biosimilars-approved-in-Canada accessed 5/15/2021

Australian Biosimilar Approvals

The regulatory body for therapeutic goods in Australia is the **Therapeutic Goods Administration (TGA).**

Australian Government
Department of Health
Therapeutic Goods Administration

Once licensed by TGA, there is a system of cost subsidy for drugs, called the Pharmaceutical Benefits Scheme (PBS), whose role is to balance cost and the contribution of an individual drug to an improved outcome for patients.

Aczicrit and Grandicrit (epoetin lambda) were the first products approved in Australia as biosimilars in 2010.

To date, TGA has approved **26 biosimilars** within the product classes of human growth hormone, granulocyte colony-stimulating factor, insulin, erythropoietin, follicle stimulating hormone (FSH), monoclonal antibody and tumour necrosis factor (TNF)-inhibitor.

https://gabionline.net/Biosimilars/General/Biosimilars-approved-in-Australia Accessed 5/15/2021

Latin America Biosimilar Approvals

Regulation of similar biotherapeutic products in Latin America varies widely among different countries. Although many countries have yet to introduce guidance for biosimilars, Latin America is moving towards increasing standards of regulation for these products.

For example, in recent years, ANMAT) in Argentina, ANVISA in Brazil and COFEPRIS in Mexico have developed their own abbreviated regulatory pathways for biosimilars by merging and adapting World Health Organization (WHO) and European Medicines Agency (EMA) guidelines.

To date, **23 biosimilars** for bevacizumab, epoetin alfa, etanercept, filgrastim, infliximab, interferon alfa and rituximab have been approved in Latin America.

http://www.gabionline.net/Biosimilars/General/Similar-biotherapeutic-products-approved-and-marketed-in-Latin-America accessed 2/8/2020

Summary

- Biologic medicines offer effective treatments to manage serious and chronic conditions like cancer, rheumatoid arthritis, psoriasis, and Crohn's disease.
- Biosimilars are safe and effective alternatives that offer patients new treatment options and are an important tool for private and government payors to help control health costs.
- Because (unlike generics) they are not identical to their reference products, their safe implementation poses some policy challenges which we will examine.
- These include ensuring strong pharmacovigilance, concerns over the switching of stable patients, mandatory switches, promoting competition, and ensuring long-term sustainability of biosimilar markets.
- As the number of approved and marketed biosimilars continues to increase, addressing these questions will become increasingly important.

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Thank You For Your Attention