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Evolving biosimilars landscape

An overview of market dynamics and future outlook for biosimilars

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Agenda

1. Regulatory landscape of biosimilars in key markets
2. Global biosimilar development landscape
3. Drivers of and barriers to biosimilar uptake
4. Future expectations for the biosimilars market

1. Regulatory landscape of biosimilars in key markets

Defining a biosimilar

- Biosimilar drugs are **similar** to the originator product.
  - Biological products cannot be fully characterized owing to their size and complexity.
  - Each manufacturing process produces a slightly different biological product.

US legislation defines biosimilarity to mean:

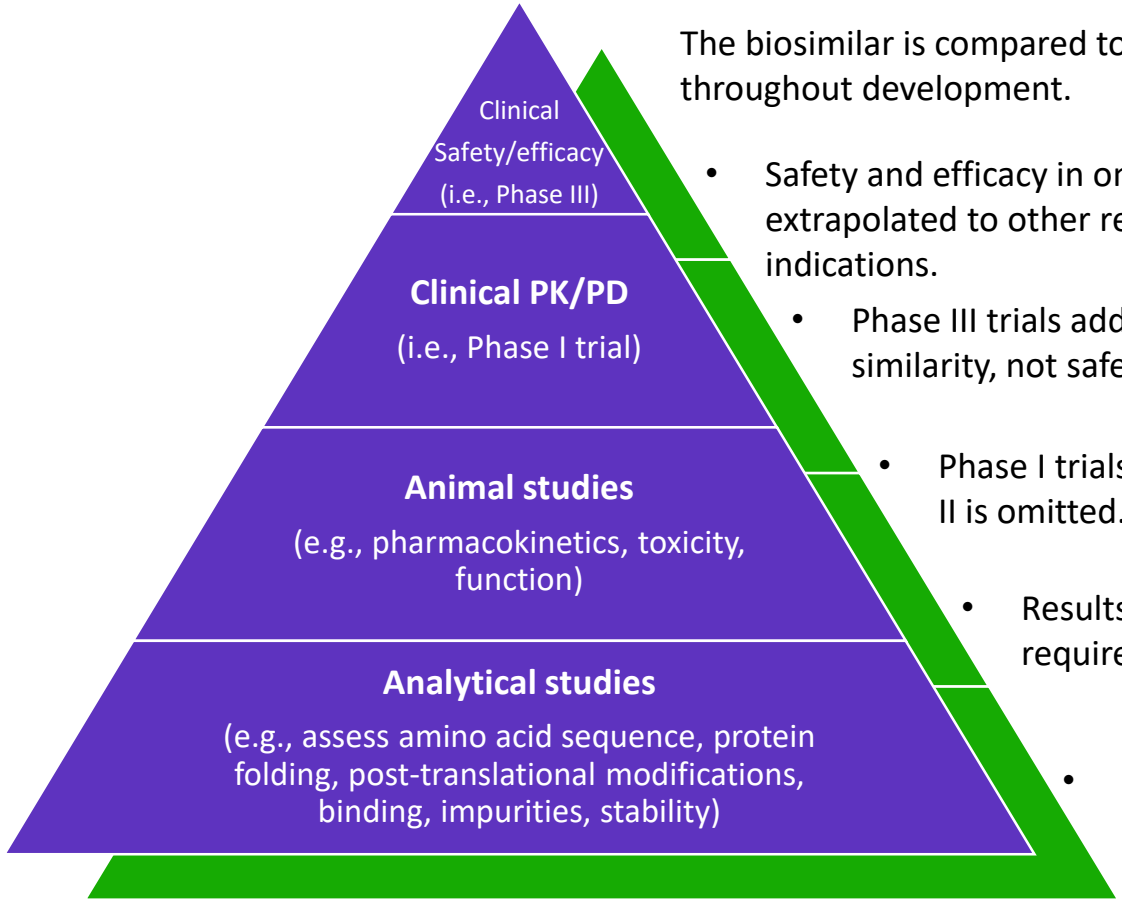
- "That the biological product is **highly similar** to the reference product notwithstanding minor differences in **clinically inactive components**"

And that:

- "There are **no clinically meaningful differences** between the biological product and the reference product in terms of the **safety, purity, and potency** of the product.

How to demonstrate "no clinically meaningful differences"

Totality of Evidence Approach

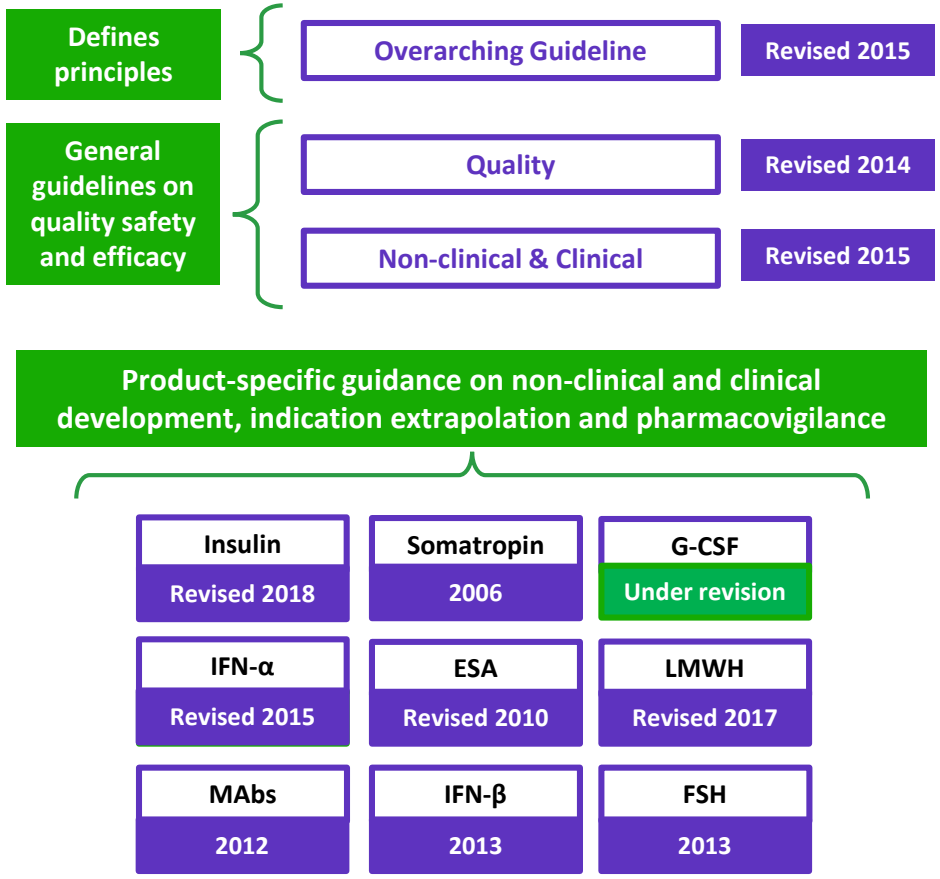


The biosimilar is compared to the reference product throughout development.

- Safety and efficacy in one indication can be extrapolated to other reference-product indications.
  - Phase III trials address residual uncertainty about similarity, not safety and efficacy, per se.
- Phase I trials are required, but Phase II is omitted.
- Results of each stage determine the requirements of the next stage.
- Step-wise process.

Source: Biosimilars Guidances, FDA, 2019

EMA biosimilars guidance scope



- 3 overarching guidelines are applicable to all well-characterized biologics
  - Acceptance of data from clinical trials using reference product sourced from other ICH regions.
  - Reduces duplication of effort.
- 9 product-specific guidelines are applicable to the most relevant molecules for biosimilar development

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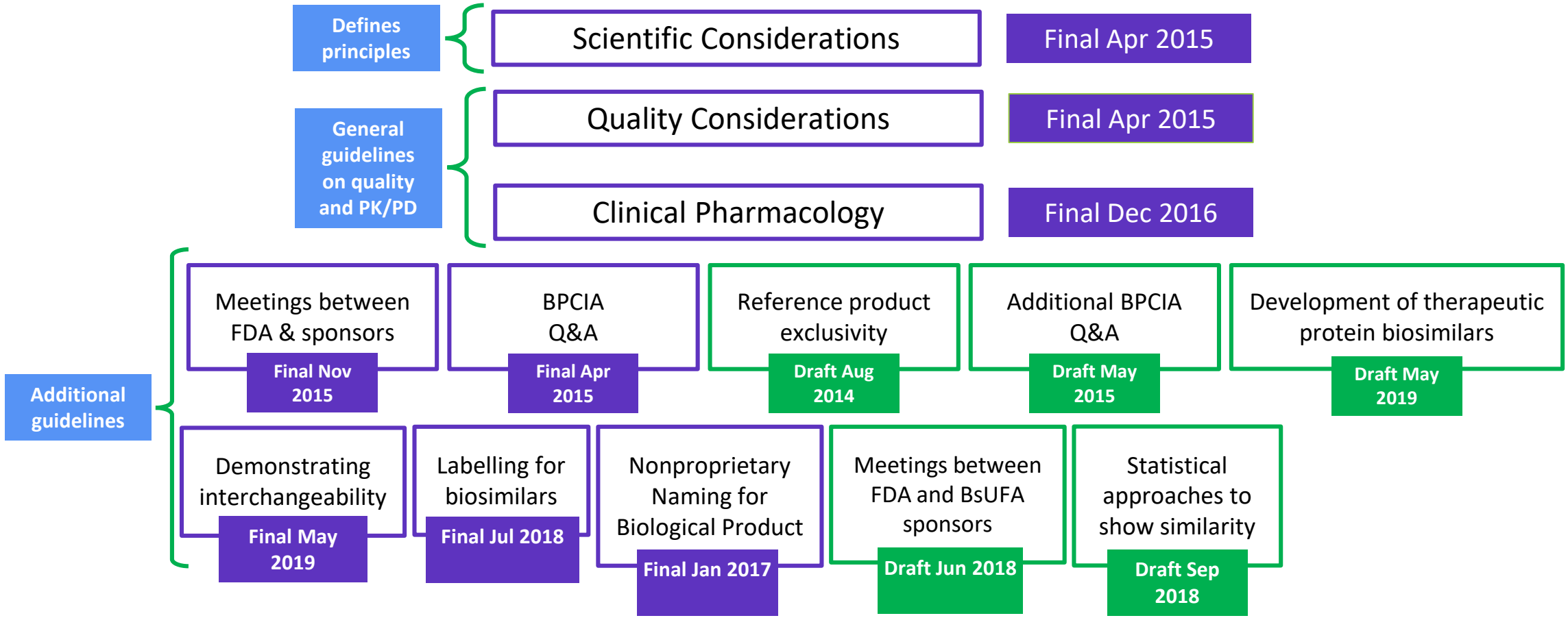
Source: Biosimilars | Access & Reimbursement Global Landscape, DRG, part of Clarivate, 2020

FDA guidance for the 351(k) biosimilars pathway



Source: Biosimilars | Access & Reimbursement Global Landscape, DRG, part of Clarivate, 2020

Biosimilar regulation in other key markets

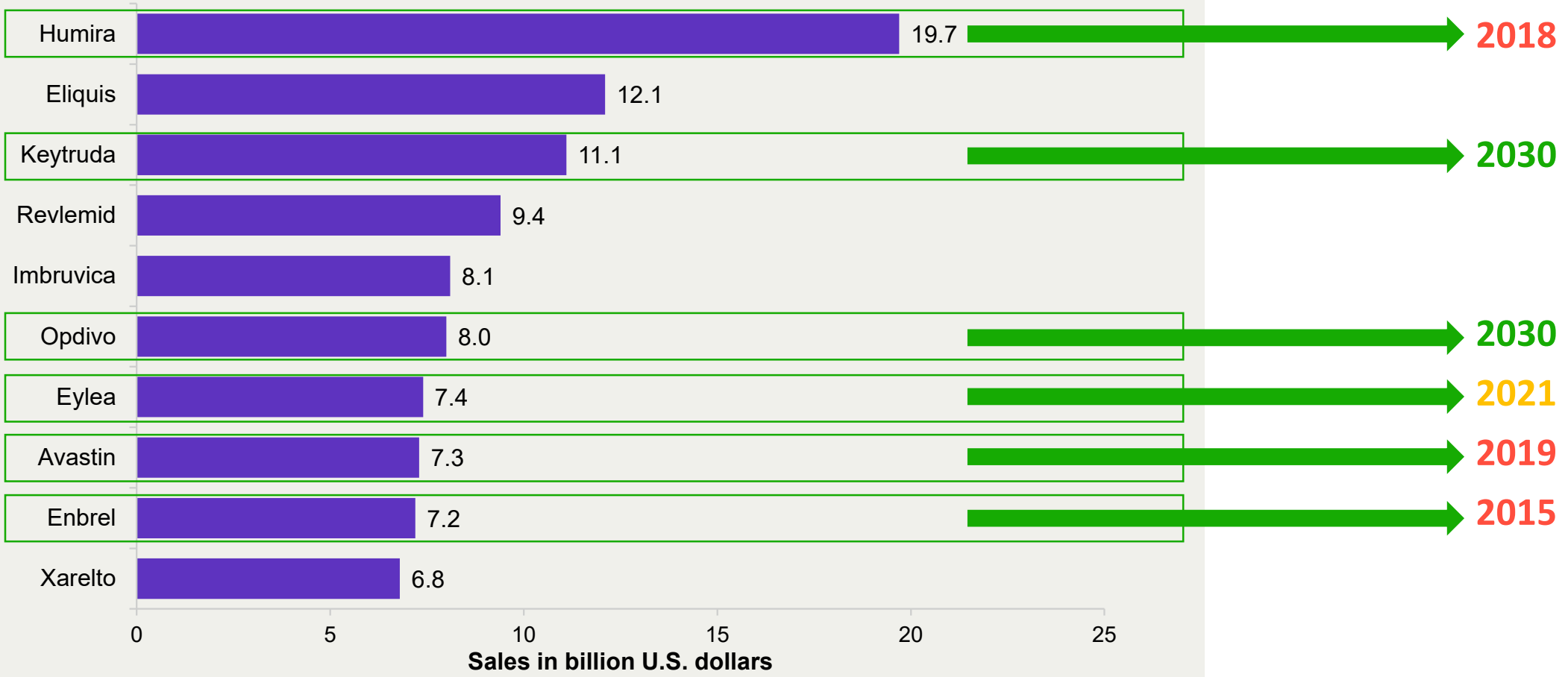
Country	Year of regulation launched	Comparative clinical trials required	Allowance of Biosimilar Automatic Substitution
Japan	2009 (final)	Yes	No
South Korea	2009 (final)	Yes	No
China	2015 (final)	Yes	No
Australia	2013 (final)	Yes	Yes (on a case-by-case basis)
Canada	2010 (final)	Yes	No
Brazil	2010 (final)	Yes	No (however, ANVISA are currently exploring biosimilar interchangeability)
India	2012 (final, updated in 2016)	Yes	Unclear in guidelines
Russia	2014 (draft)	Yes	Yes (on a case-by-case basis)

Source: Biosimilars | Access & Reimbursement Global Landscape, DRG, part of Clarivate, 2020

2. Global biosimilar development landscape

Commercial opportunity for biosimilars

Top 10 drugs by sales worldwide in 2019 (in billion U.S. dollars)



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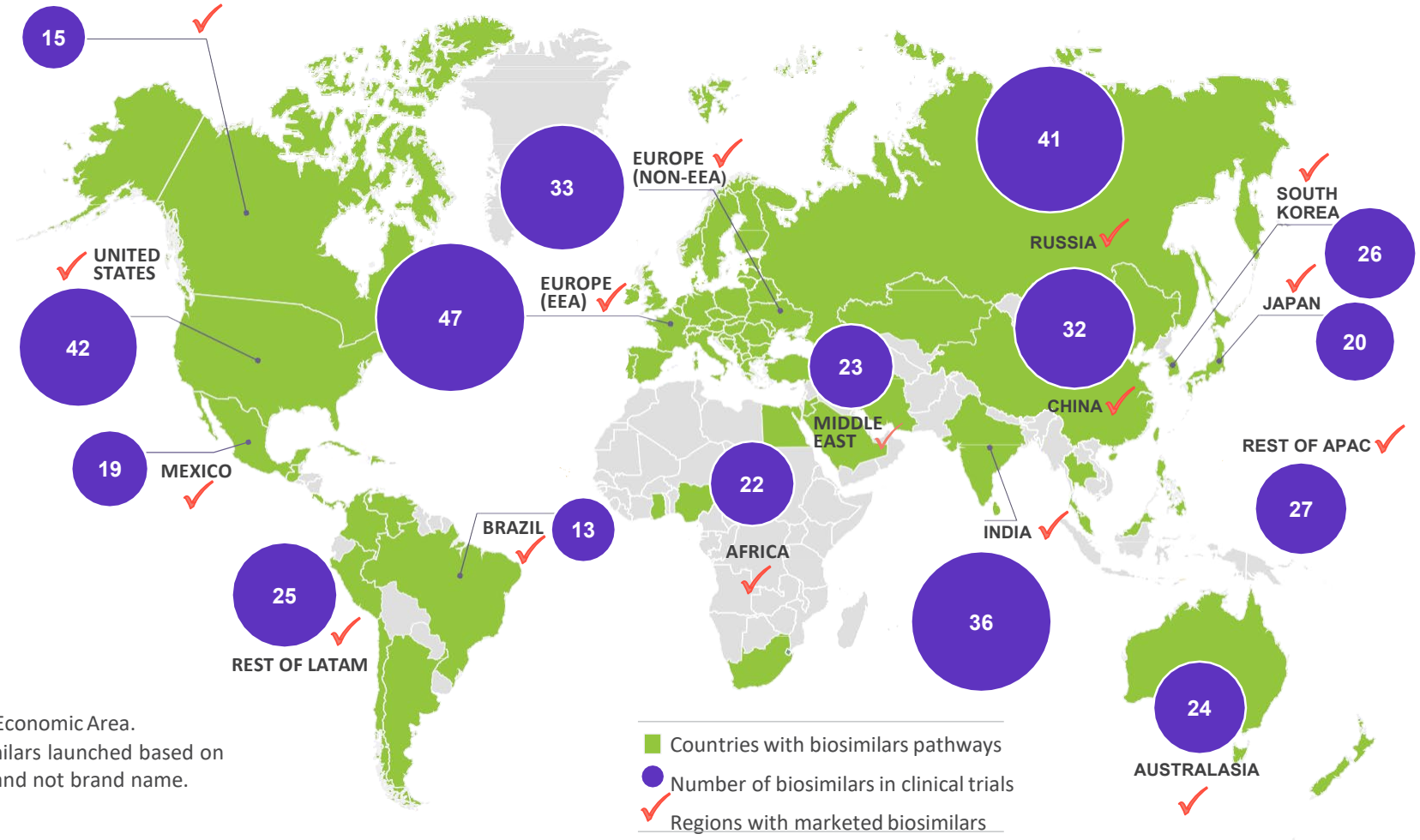
Source: Company & Drug, DRG, part of Clarivate, 2020

Global biosimilars clinical development activity

Where are the biosimilar hot spots?



EEA = European Economic Area.

[1] Count of biosimilars launched based on molecule name and not brand name.

19

BIOSIMILAR MOLECULES LAUNCHED IN THE UNITED STATES

37

BIOSIMILAR MOLECULES LAUNCHED IN EUROPE

25%

ANNUAL INCREASE IN APPROVED BIOSIMILARS, GLOBALLY

>400

BIOSIMILARS IN DEVELOPMENT, GLOBALLY

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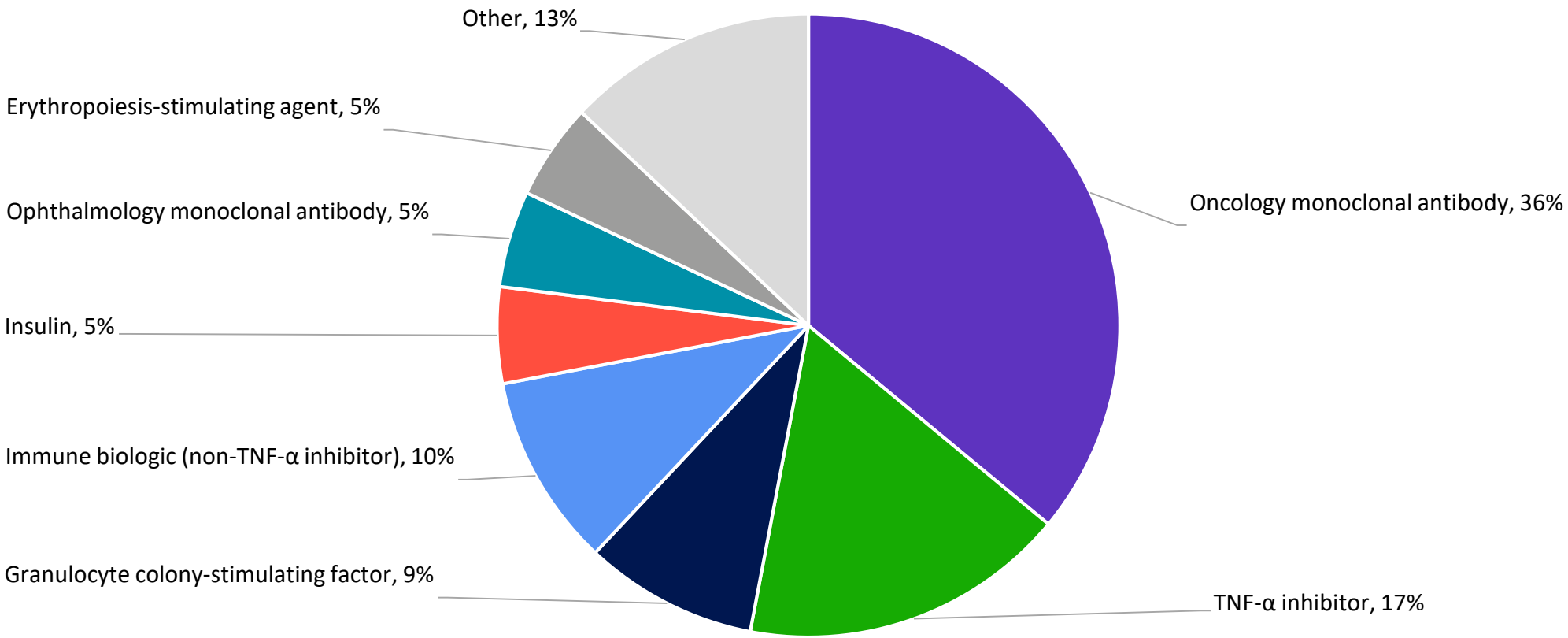
Source: Emerging Biosimilars, DRG, part of Clarivate, 2020

Biosimilars development pipeline by class

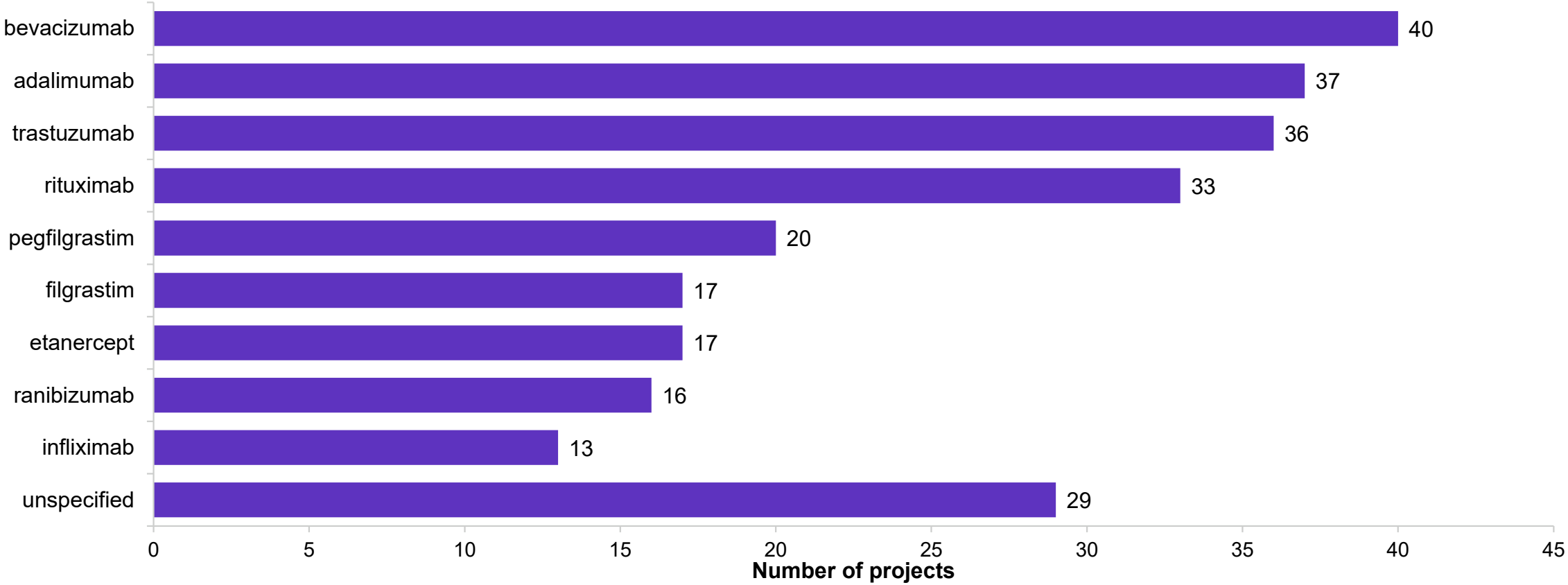
The classes of biologics most frequently targeted by biosimilars developers are oncology monoclonal antibodies (36%), followed by TNF-α inhibitors which are used in autoimmune indications (17%).



Source: Emerging Biosimilars, DRG, part of Clarivate, 2020

Biosimilar development projects by reference molecule

The top molecules most often targeted by biosimilars developers are from oncology and immunology therapy areas – bevacizumab (Avastin), adalimumab (Humira), and trastuzumab (Herceptin), and rituximab (Rituxan / MabThera).



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Source: Emerging Biosimilars, DRG, part of Clarivate, 2020

3. Drivers of and barriers to biosimilar uptake

Key drivers and barriers to biosimilars market growth

Continuation biologics **patent "cliff"**

Pressure on healthcare systems to **contain healthcare costs**

Technological advances in biologics analytics and manufacturing, including lower-cost production

Complexity of development and shifting regulatory requirements

Physician caution in adopting biosimilars, particularly in patients already receiving the reference brand

Relatively **small savings** compared with small-molecule generics

A current **lack of pharmacy-level substitution** for biologics

Limited presence of cohesive payer strategies to drive uptake of biosimilars at a national level

Perceptions of top drivers and barriers of biosimilar use:

Physicians and payers

- Lower cost to payers, institutions & clinics, and familiarity & experience with biosimilars, are top drivers of biosimilar use.
- Lack of efficacy, safety, & insufficient cost benefit to healthcare systems & payers are perceived as top barriers to biosimilar use.

Rx	Rx
1. Lower costs to payers	1. Efficacy
2. Lower cost to institutions or clinics	2. Concerns about the lack of long-term clinical data / less data overall compared to brands
3. Physicians familiarity/comfort with biosimilars	3. Insufficient cost benefit to healthcare system / payers

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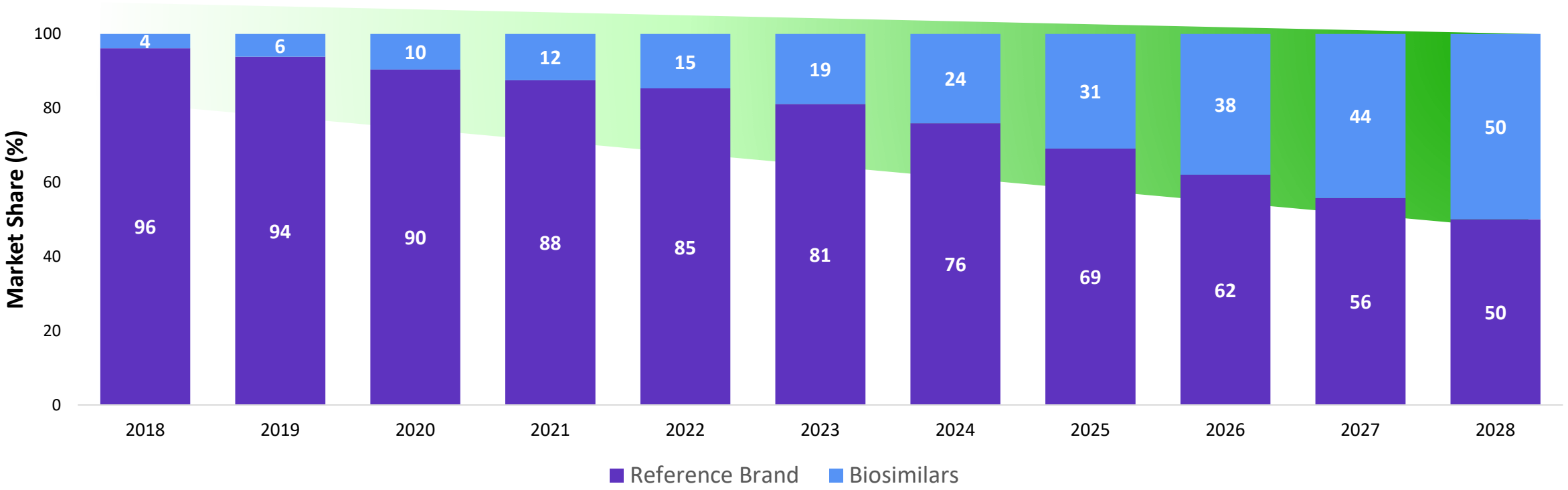
Sources: Biosimilars | Current Treatment Landscape, Biosimilars | Access & Reimbursement | Payer Insights US/EU5, DRG, part of Clarivate, 2020

4. Future expectations for the biosimilars market

Major-market shares of reference brands and biosimilars

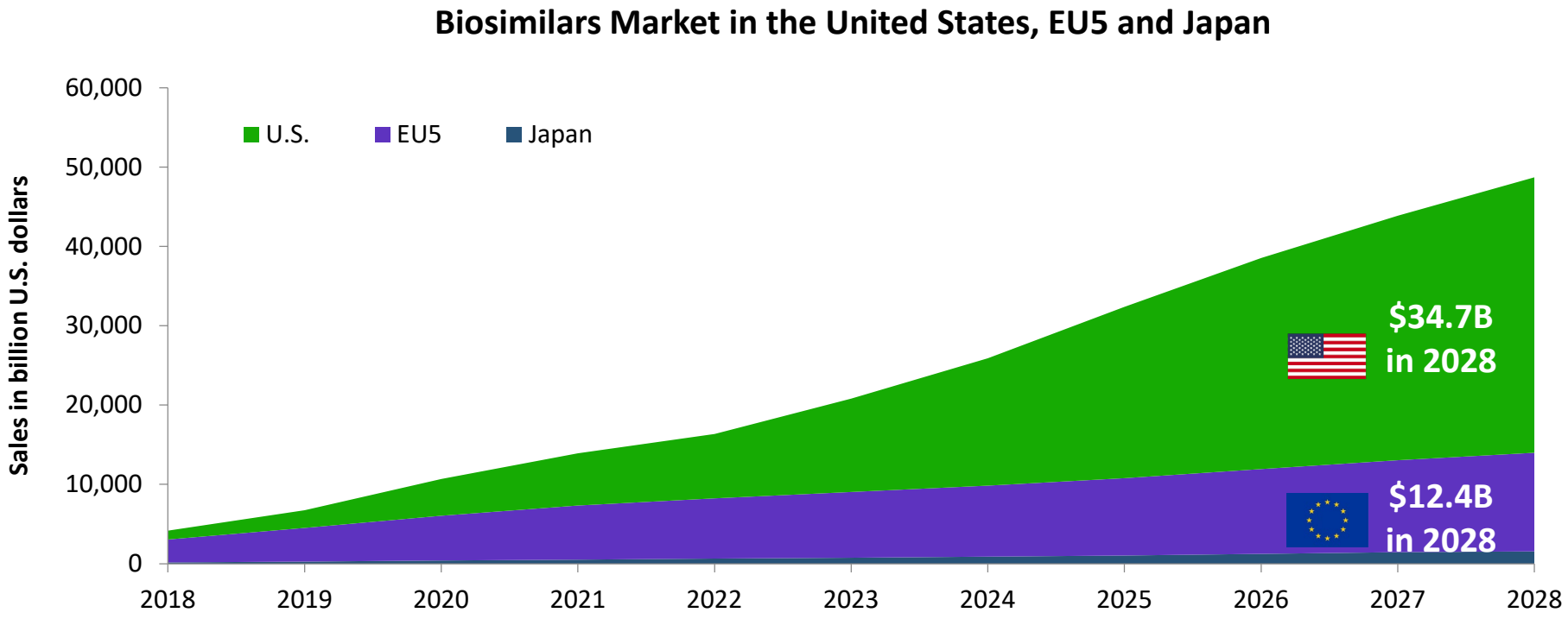
- The entry and growing adoption of biosimilars in the major markets will contribute to a reduction in growth, and eventually a decline, of the reference brands through to 2028.
- The lower ex-manufacturer cost of biosimilars compared with reference brands and the expectation of further discounts will contribute to a 28% CAGR market opportunity for biosimilars during the 2018-2028 forecast period.



Source: Biosimilars | Market Events & Forecast, DRG, part of Clarivate, 2020

Outlook for biosimilar sales in major markets

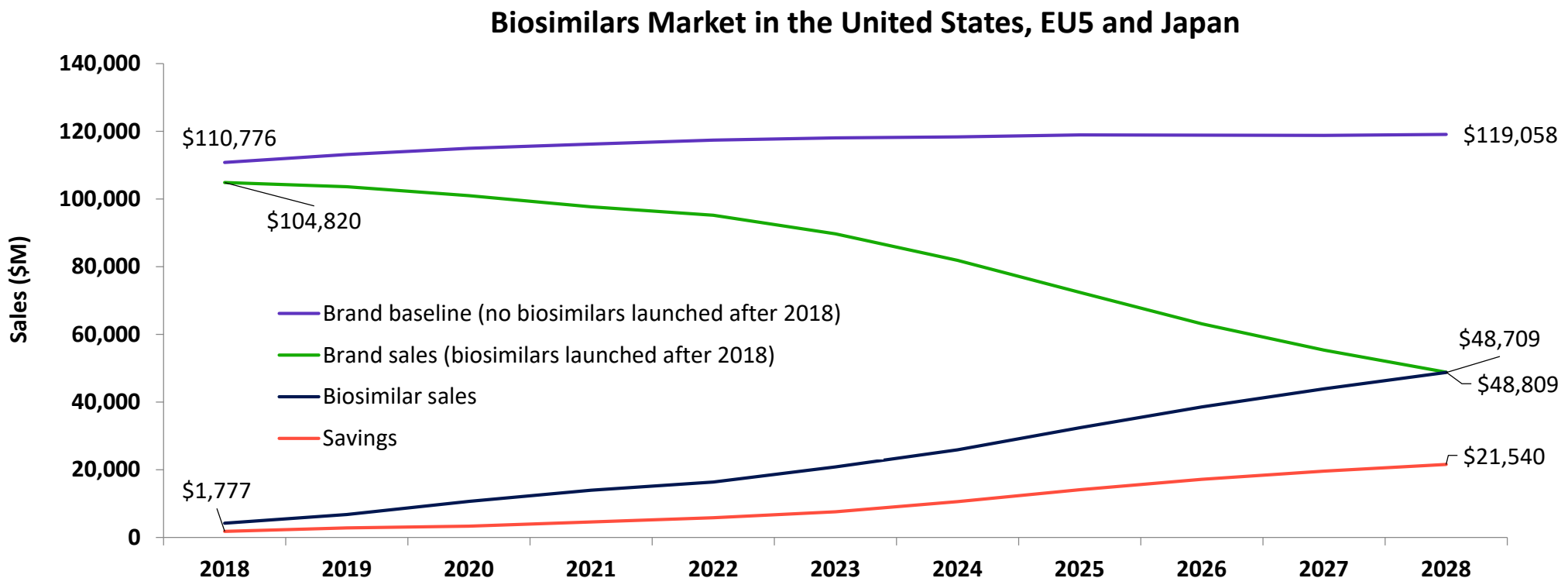
Overall in the seven major markets we forecast, we expect biosimilars for over 20 branded biologics that do not currently face biosimilar competition in any of the major markets, leading to a significant increase in sales from 2022 onwards.



Source: Biosimilars | Market Events & Forecast, DRG, part of Clarivate, 2020

Outlook for biosimilar sales in major markets

- Across the major markets, biosimilars of the reference brands covered in our bottom-up forecast analyses will erode reference-brand sales (at the ex-manufacturer price) by $70.3 billion in 2028, saving $21.5 billion in the process.



Source: Biosimilars | Market Events & Forecast, DRG, part of Clarivate, 2020

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