2021 BIOSIMILAR TRENDS REPORT

CURRENT STATE OF THE MARKETPLACE

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The United States (US) marketplace is poised to welcome many new biosimilars in 2021 and beyond, spurring additional competition that will potentially lead to significant savings for the healthcare system, which can then be deployed to newer, innovative treatments.[1,2]

Over the past couple of years, US regulatory agencies have developed policies that maintain a level playing field for biosimilars and reference products.

> **We anticipate that market share rates will continue to rise through 2021 as a result of more adoption among providers and sites of care. Studies show that costs could decrease by nearly 30% if biosimilar uptake continues at the current rate.[3]**
>
> **– Sean McGowan, Senior Director of Biosimilars, AmerisourceBergen**

Essential components of provider and patient use of biosimilars include addressing the clinical, operational, and economic considerations to drive adoption as well as payer coverage.[4-6]

Biosimilar adoption is one of many measures of success. Reference products may also lower prices to compete. This is a positive outcome that results from biosimilar competition.[7]

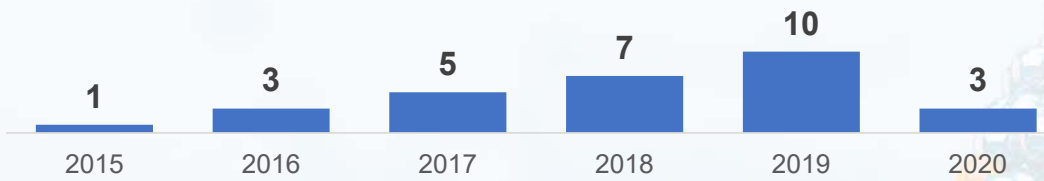
While financial savings are important for driving biosimilar uptake, they are not the only consideration for payers and providers. Other factors include manufacturer reputation for producing high-quality products, reliably supplying these products, and understanding provider and payer clinical, economic, and operational needs and decision-making drivers.[8-10]

CURRENT STATE OF THE MARKETPLACE

Comparison to Previous Year, 6-Year Trend

The US marketplace for biosimilars is now well-established and accelerating across multiple therapeutic areas. In 2018, the Food and Drug Administration (FDA) approved 7 biosimilars, which brought the total approvals to 16. In 2019, the FDA approved 10 biosimilars, bringing the total to 26 in the US.[11] **Figure 1** shows the number of biosimilars approved each year from 2015 to 2020. The steadily increasing number shows the growing strength of US biosimilars. The FDA approved 3 biosimilars in 2020.[11] The COVID-19 pandemic and the resulting shutdown most likely contributed to the slowdown of biosimilar approvals, but another wave is expected in the future.

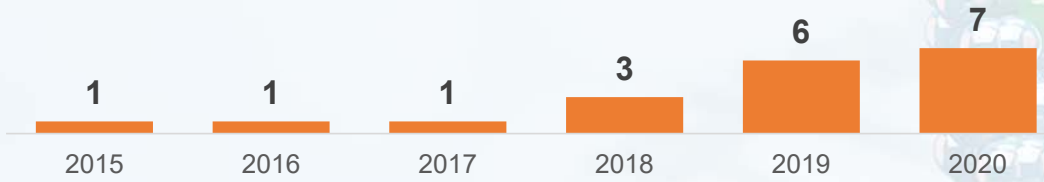
Figure 1. Number of Approved Biosimilars in the US, per Year[11]



Total Number of Approved Biosimilars: **29**

In addition, more biosimilars are becoming available to patients. By the end of 2018, there were only a total of 6 biosimilars available. In 2019, 6 more biosimilars became available, followed by another 7 in 2020.[12] **Figure 2** shows the dramatic increase in available biosimilars in 2019 and 2020 compared to prior years.

Figure 2. Number of Biosimilars Becoming Available in the US, per Year[12]



Total Number of Available Biosimilars*: **20**

Key: US – United States.
*Note: As of April 2021, there has been 1 biosimilar becoming available in 2021.[12.]

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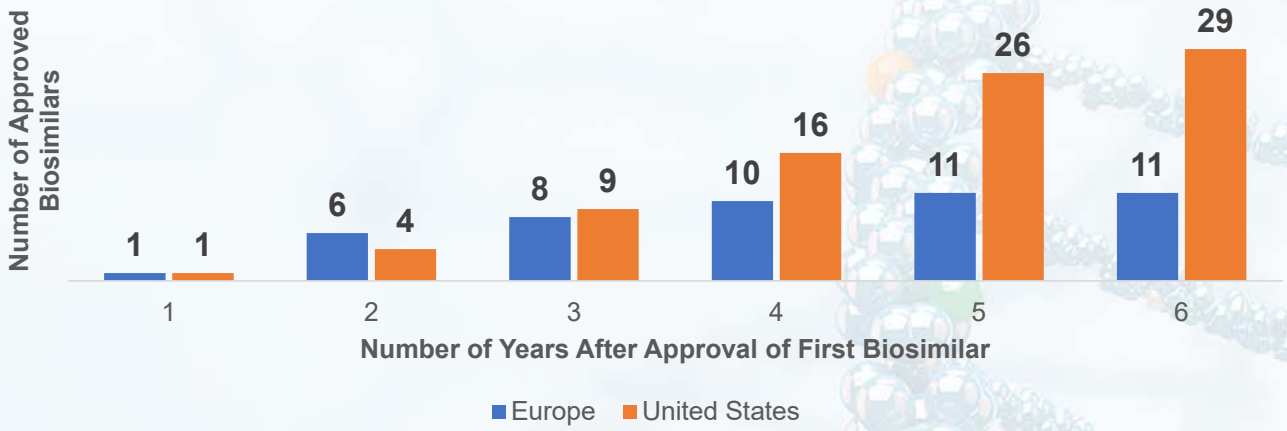
Comparison to the EU

Current data show that the US biosimilar landscape is advancing faster than the European Union (EU) biosimilar landscape during a comparable period of time. In the 6 years after the EU approved the first biosimilar (2006), there were 11 approved biosimilars. By contrast, in the first 6 years after the US approved the first biosimilar, there were 29 approved biosimilars—more than twice the number in the EU. **Figure 3** shows that, by the end of Year 6, Europe had 11 biosimilars approved and the US had 29.[11,13]

Figure 3. Comparison of Approved Biosimilars in Europe and the US[11,13]

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



Key: EU – European Union; US – United States.

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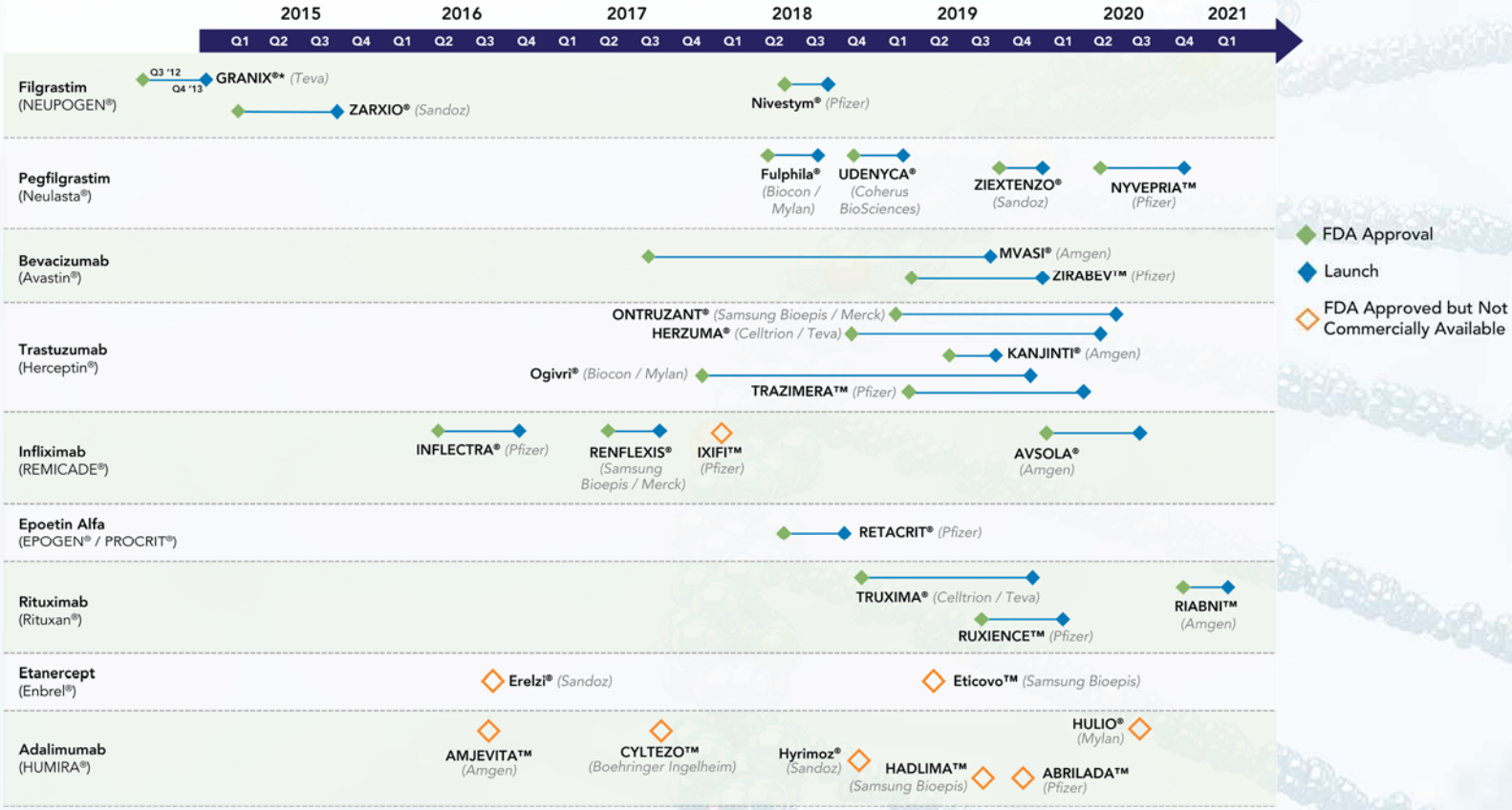
Timeline of Approved Biosimilars and Launch Date

As of April 2021, the FDA has approved **29** biosimilars and **20** biosimilars have been launched in the US as shown in **Figure 4**. Currently, there are **9** reference products that have approved biosimilars, of which **7** are available.[12]

Figure 4. Approved and Launched Biosimilars (including GRANIX*) in the US[12,14,15]



Key: FDA – Food and Drug Administration; US – United States.
*GRANIX is not a biosimilar. It was approved under a full Biologics License Application, which was submitted to the FDA before enactment of the biosimilar approval pathway.
Please see pages 12–16 for Boxed Warning information for AVSOLA, EPOGEN, ENBREL, KANJINTI, and RIABNI.

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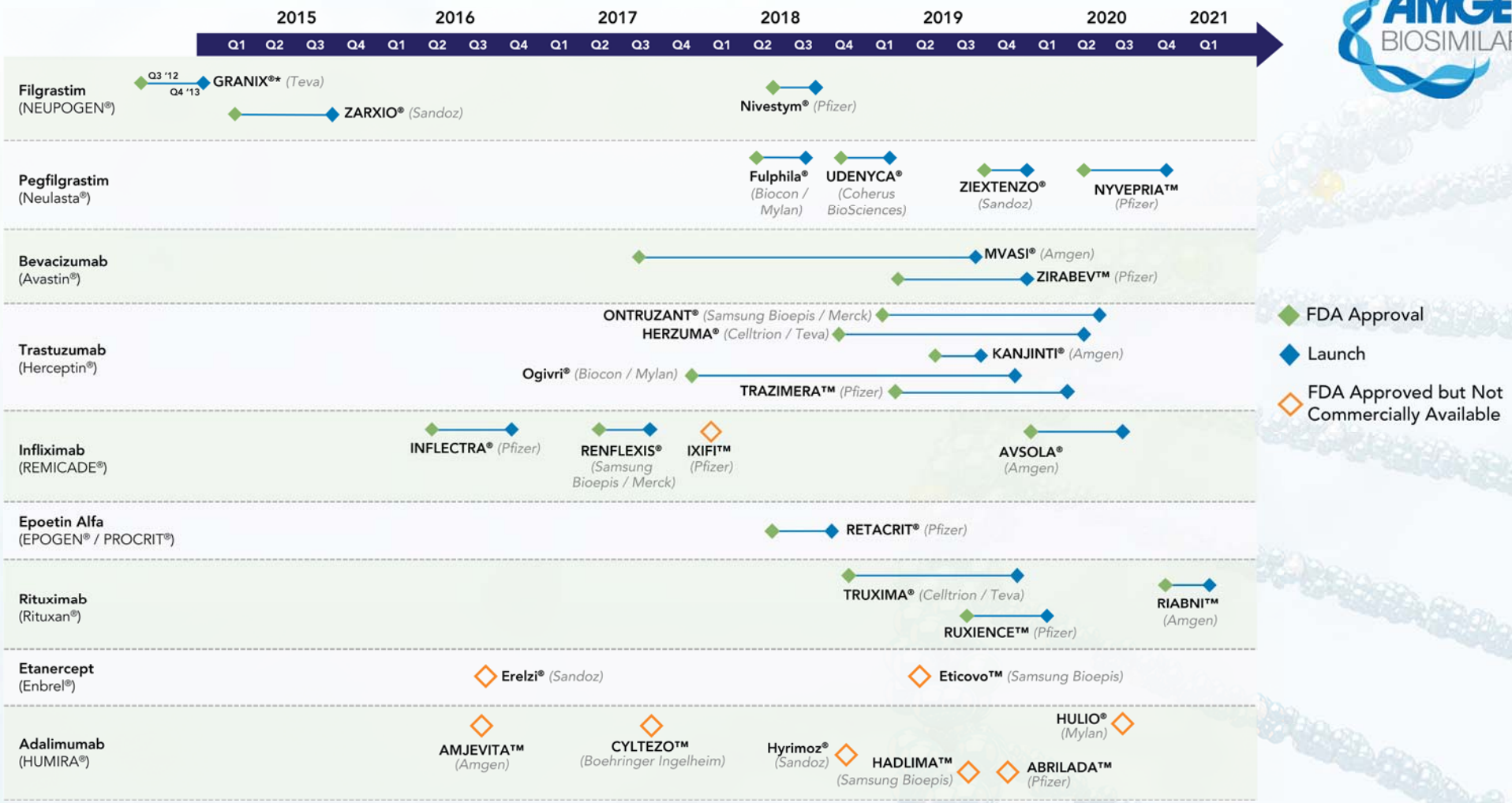

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Biosimilars Launch With Significant Discounts to WAC and ASP

Biosimilars are reducing healthcare costs by providing significant wholesale acquisition cost (WAC) and average sales price (ASP) savings at launch and through price competition, resulting in additional savings over time.

As shown in **Figure 5**, manufacturers are launching biosimilars at a WAC price that is generally lower than the reference product[16] (biosimilars' ASP becomes available 2 full quarters after launch.)[17]

Biosimilars launch at a WAC price that is generally

15% to 37% lower than the reference product[16]

To date, almost all biosimilars have launched at a WAC price

3% to 24% below the reference product ASP[16]

Key: ASP – average sales price; Bio – biosimilar; RP – reference product; WAC – wholesale acquisition cost.
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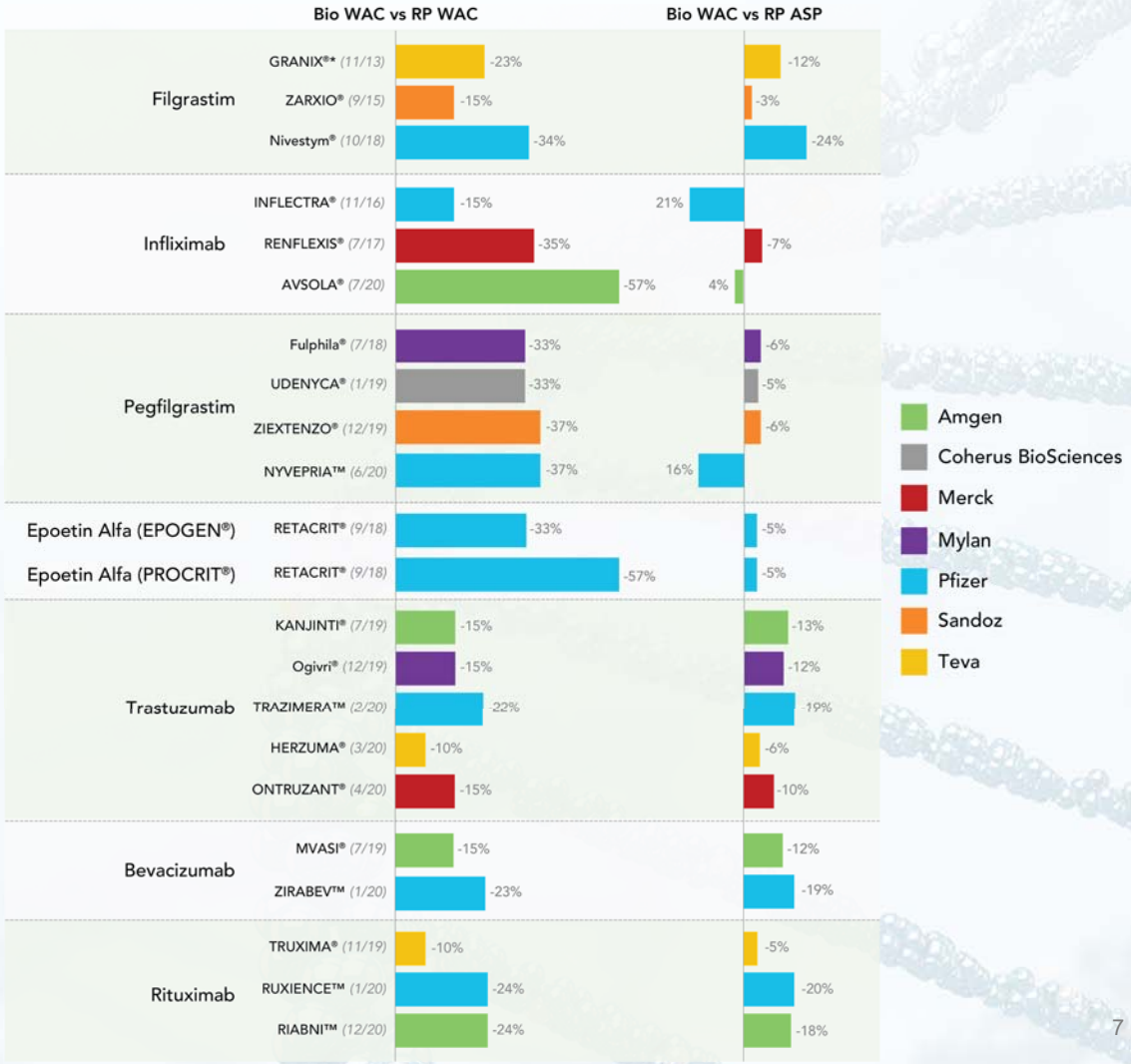
Figure 5. Price at Launch vs Reference Product[16]



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ASP of Reference Products Are Declining

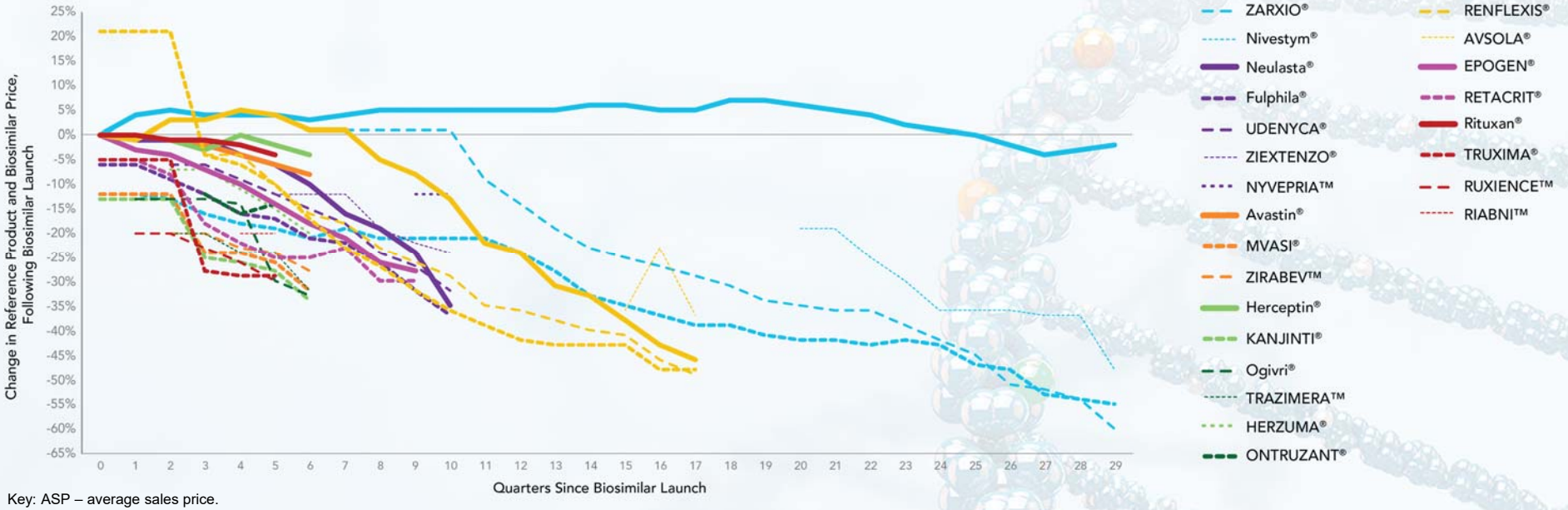
As expected, competition results in lower ASP for both reference products and biosimilars, leading to additional savings. As shown in **Figure 6**, in most cases, the prices of biosimilars decline once ASP is established and continue a steady downward trend.[16] The ASPs for reference products are also declining over time, leading to further healthcare savings.

The prices of biosimilars are decreasing at a CAGR of

10% to 15%

Figure 6. Downward Trend in ASP for Biosimilars and Reference Products Over Time[16]

Cost-Savings in Biosimilar vs Reference Product



Key: ASP – average sales price.
*NEUPOGEN®'s biosimilar price-response strategy focused on account-level provider contracting. This targeted approach modestly increased the ASP-eligible discount rate, resulting in a more stable ASP trend.
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Source: Analysource.
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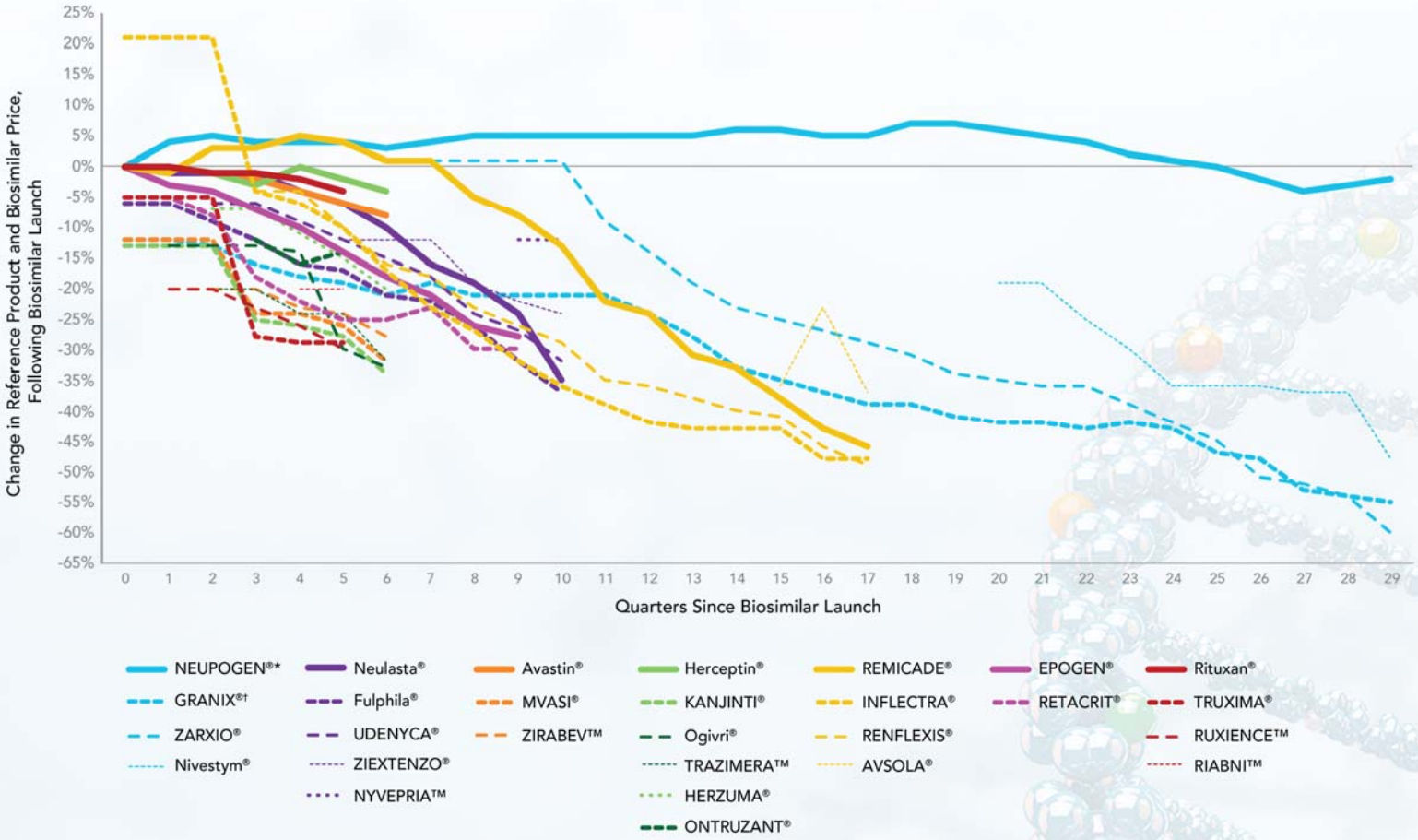

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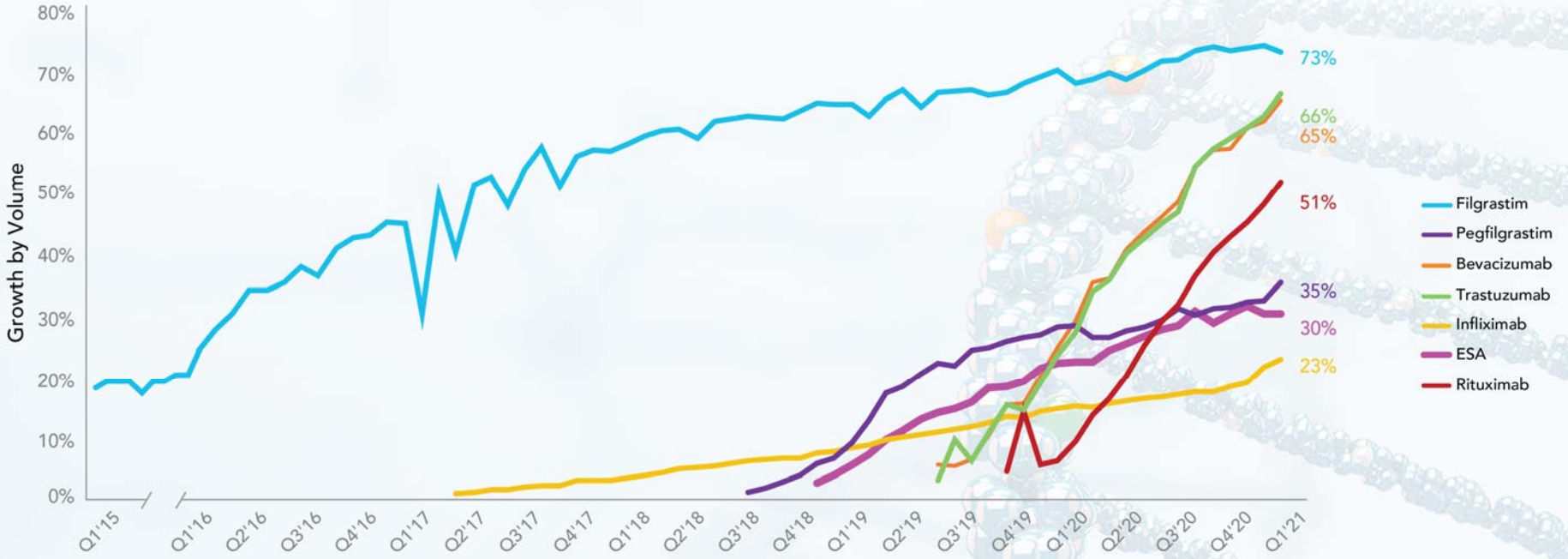
Growth in Biosimilar Uptake

The rate of biosimilar uptake is generally increasing over time, as depicted in **Figure 7**.[18] Biosimilars have gained significant share in the majority of therapeutic areas where they have been introduced. Additionally, first-to-launch biosimilars tend to capture a greater portion of the segment compared to later entrants.

For therapeutic areas with biosimilars launched in the last two years, the average share is **61%**

For therapeutic areas with biosimilars launched prior to 2019, the average share after two years was **13%**

Figure 7. Biosimilar Growth Uptake Curve[18]



Key: ESA – erythropoiesis-stimulating agent.
Source: OBU Customer Data Pack Weekly (IQVIA DDD + Chargeback).

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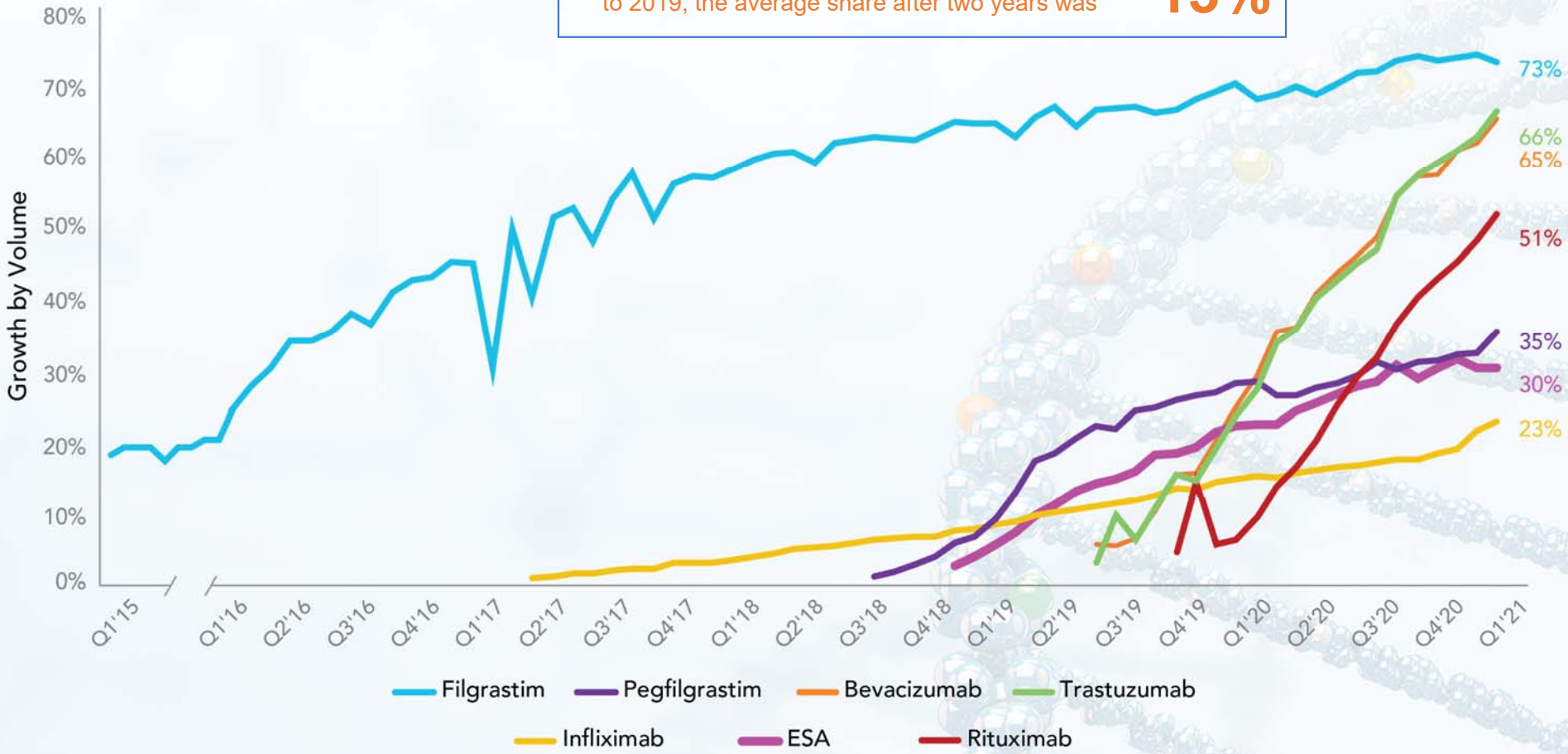

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BOXED WARNINGS

AVSOLA®

WARNING: SERIOUS INFECTIONS and MALIGNANCY

See Full Prescribing Information for complete boxed warning.

- Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis) and infections due to other opportunistic pathogens.
- Discontinue AVSOLA if a patient develops a serious infection.
- Perform test for latent TB; if positive, start treatment for TB prior to starting AVSOLA. Monitor all patients for active TB during treatment, even if initial latent TB test is negative. (5.1)
- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including infliximab products.
- Postmarketing cases of fatal hepatosplenic T-cell lymphoma (HSTCL) have been reported in patients treated with TNF-blockers including infliximab products. Almost all had received azathioprine or 6-mercaptopurine concomitantly with a TNF-blocker at or prior to diagnosis. The majority of cases were reported in patients with Crohn's disease or ulcerative colitis, most of whom were adolescent or young adult males. (5.2)

BOXED WARNINGS (cont.)

EPOGEN®

WARNING: ESAs INCREASE THE RISK OF DEATH, MYOCARDIAL INFARCTION, STROKE, VENOUS THROMBOEMBOLISM, THROMBOSIS OF VASCULAR ACCESS AND TUMOR PROGRESSION OR RECURRENCE

See full prescribing information for complete boxed warning.

Chronic Kidney Disease:

- In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL (5.1).
- No trial has identified a hemoglobin target level, ESA dose, or dosing strategy that does not increase these risks.
- Use the lowest Epogen dose sufficient to reduce the need for red blood cell (RBC) transfusions (5.1).

Cancer:

- ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers (5.2).
- Use the lowest dose to avoid RBC transfusions (2.4).
- Use ESAs only for anemia from myelosuppressive chemotherapy (1.3).
- ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure (1.5).
- Discontinue following the completion of a chemotherapy course (2.4).

Perisurgery:

- Due to increased risk of Deep Venous Thrombosis (DVT), DVT prophylaxis is recommended (5.1).

BOXED WARNINGS (cont.)

ENBREL®

WARNINGS: SERIOUS INFECTIONS AND MALIGNANCIES

See full prescribing information for complete boxed warning.

SERIOUS INFECTIONS

- Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. (5.1)
- Enbrel should be discontinued if a patient develops a serious infection or sepsis during treatment. (5.1)
- Perform test for latent TB; if positive, start treatment for TB prior to starting Enbrel. (5.1)
- Monitor all patients for active TB during treatment, even if initial latent TB test is negative. (5.1)

MALIGNANCIES

- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including Enbrel. (5.3)

BOXED WARNINGS (cont.)

KANJINTI®

WARNING: CARDIOMYOPATHY, INFUSION REACTIONS, EMBRYO-FETAL TOXICITY, and PULMONARY TOXICITY

See full prescribing information for complete boxed warning.

Cardiomyopathy: Trastuzumab products can result in subclinical and clinical cardiac failure manifesting as CHF, and decreased LVEF, with greatest risk when administered concurrently with anthracyclines. Evaluate cardiac function prior to and during treatment. Discontinue KANJINTI for cardiomyopathy. (2.3, 5.1)

Infusion Reactions, Pulmonary Toxicity: Discontinue KANJINTI for anaphylaxis, angioedema, interstitial pneumonitis, or acute respiratory distress syndrome. (5.2, 5.4)

Embryo-Fetal Toxicity: Exposure to trastuzumab products during pregnancy can result in oligohydramnios, in some cases complicated by pulmonary hypoplasia and neonatal death. Advise patients of these risks and the need for effective contraception. (5.3, 8.1, 8.3)

BOXED WARNINGS (cont.)

RIABNI™

WARNING: FATAL INFUSION-RELATED REACTIONS, SEVERE MUCOCUTANEOUS REACTIONS, HEPATITIS B VIRUS REACTIVATION and PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY

See full prescribing information for complete boxed warning.

- Fatal infusion-related reactions within 24 hours of rituximab infusion; approximately 80% of fatal reactions occurred with first infusion. Monitor patients and discontinue RIABNI infusion for severe reactions (5.1).
- Severe mucocutaneous reactions, some with fatal outcomes (5.2).
- Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death (5.3).
- Progressive multifocal leukoencephalopathy (PML) resulting in death (5.4).

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