



# 2021 BIOSIMILAR TRENDS REPORT

START >

# TABLE OF CONTENTS



<b>● Introduction and Report Overview</b>	>
Foreword: A Word From Our VP of US Value and Access	4
About Amgen	5
2021 Biosimilar Trends Report Key Takeaways	6
<b>● Current State of the Marketplace</b>	>
Trends in US Biosimilar Approvals and Launches	9
Timeline of Approved Biosimilars and Launch Dates	11
Trends in ASP, Uptake, and Total Drug Spend	12
Boxed Warnings for Amgen Products	16
<b>● Future State of the Marketplace</b>	>
The Future of Biosimilars in the US	19
The Future of Autoimmune Therapies	20
Lessons for the Future From Real-World Evidence	22
Important Considerations for the Future	25
<b>● Trends</b>	>
Oncology Therapeutics	27
Oncology Supportive Care	43
Nephrology/Oncology Supportive Care	53
Inflammation	59
<b>● Stakeholder Considerations</b>	>
Healthcare Systems	66
Providers	67
Payers and Employers	72
Patients	76
<b>● Reimbursement</b>	>
<b>● Policy Update</b>	>
<b>● Understanding Biosimilars</b>	>
<b>● References</b>	>



# INTRODUCTION AND REPORT OVERVIEW

- > Foreword: A Word From Our VP of US Value and Access
- > About Amgen
- > 2021 Biosimilar Trends Report Key Takeaways

- INTRODUCTION AND REPORT OVERVIEW

Foreword: A Word From Our VP of US Value and Access

About Amgen

2021 Biosimilar Trends Report Key Takeaways

- CURRENT STATE OF THE MARKETPLACE

- FUTURE STATE OF THE MARKETPLACE

- TRENDS

- STAKEHOLDER CONSIDERATIONS

- REIMBURSEMENT

- POLICY UPDATE

- UNDERSTANDING BIOSIMILARS

- REFERENCES



# FOREWORD

## A word from our Vice President of US Value and Access

Dear Colleagues,

We are pleased to share with you the 8th edition of our **Biosimilar Trends Report**.

What we've observed over the past 8 years of analysis is that increasing biosimilar availability and adoption is delivering on the fundamental promise of reducing healthcare costs for payers, employers, and patients.

To date, 30 biosimilars\* have received regulatory approval, and 21 products have been launched.<sup>1</sup> Entering the marketplace at prices ranging 15% to 37% lower than reference products, biosimilars have increased competition, gained significant share, and created savings to the healthcare system to the tune of \$9.8 billion over the past 5 years.<sup>2,3</sup> Importantly, these developments translated into significant savings for patients, estimated at \$238M of out-of-pocket savings per year.<sup>4</sup>

As described in the "Policy Update" section of this report, regulators, policy makers, and patients/advocacy groups continue to play an important role in driving understanding, reimbursement, acceptance, and adoption of biosimilars in the healthcare system. Thanks to these efforts, in the immediate future we expect significant advancements, including (1) biosimilar entrances in more therapeutic areas and (2) the expansion of biosimilars into pharmacy benefit reimbursement.

With large investments across a portfolio of 10 biosimilar medicines – a far larger stake than most of our peers – Amgen is dedicated to fostering a sustainable marketplace for patients and the healthcare system.

We encourage you to explore key trends on biosimilar adoption within this report, including analyses across multiple therapeutic areas.



**Jen Norton**  
Vice President  
US Value and Access, Amgen

● INTRODUCTION AND REPORT OVERVIEW

Foreword: A Word From Our VP of US Value and Access

About Amgen

2021 Biosimilar Trends Report Key Takeaways

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



Key: US – United States.

\*Throughout this report, unless otherwise noted, the term "biosimilars" refers to biological products licensed under 351(k) of the Public Health Service Act.

# ABOUT AMGEN



When the Biologics Price Competition and Innovation Act (BPCIA) was enacted in the US in 2010, creating the biosimilars approval pathway, we embraced the opportunity to extend our mission to serve patients. We recognized that biosimilars would become an important part of broadening patient and physician options for biologic treatments and foresaw that our expertise in developing and manufacturing originator biologics would also apply to biosimilars.

Starting with that premise, we have invested more than \$2 billion across our portfolio of 10 biosimilar candidates and marketed products intended to target serious diseases. We have reached a unique position – we have a deep and growing portfolio of innovator products, as well as an already-successful commitment to developing and marketing biosimilars. With multiple US approvals and launches of biosimilars, we have a far larger stake than most companies entering the marketplace with biosimilars.

Our high-quality biosimilars can potentially offer more affordable options that contribute to the sustainability of our healthcare system and allow for greater investment in new medicines for patients. We also have unique insights and a commitment to advocate for a biologics marketplace that will promote innovation and quality, while at the same time bringing more competition and meaningful cost savings to the healthcare system.

**Founded in 1980, Amgen has grown from a biotechnology pioneer into an acknowledged leader in the development of innovative biologic medicines. We are committed to unlocking the potential of biology for patients suffering from serious illnesses by discovering, developing, manufacturing, and delivering innovative human therapeutics.**



CLICK HERE FOR ADDITIONAL INFORMATION/RESOURCES

## ● INTRODUCTION AND REPORT OVERVIEW

Foreword: A Word From Our VP of US Value and Access

About Amgen

2021 Biosimilar Trends Report Key Takeaways

## ● CURRENT STATE OF THE MARKETPLACE

## ● FUTURE STATE OF THE MARKETPLACE

## ● TRENDS

## ● STAKEHOLDER CONSIDERATIONS

## ● REIMBURSEMENT

## ● POLICY UPDATE

## ● UNDERSTANDING BIOSIMILARS

## ● REFERENCES



# 2021 BIOSIMILAR TRENDS REPORT

## Key takeaways



Since the first biosimilar entered the US marketplace in 2015, **30 products have been approved** and **21 products have been launched**.<sup>1</sup> Biosimilars have gained significant share in the majority of therapeutic areas where they have been introduced.<sup>5</sup> The US marketplace is **poised to see further growth in biosimilars approved to date and welcome many new biosimilars in the years to come**. Additional competition will potentially lead to significant savings for the healthcare system, and these savings can be deployed to newer, innovative treatments.<sup>6</sup>



The **average sales price (ASP) is declining for both reference products and biosimilars over time**. The prices of biosimilars are decreasing at a CAGR of 9% to 19%. The prices of most reference products are decreasing at a CAGR of 4% to 17%.<sup>2</sup>



The cumulative reduction in drug spend for classes with biosimilar competition is estimated to have been **\$9.8 billion over the past 5 years**.<sup>3</sup>



The next few years will likely see **several advancements** in this space:

- Expansion of biosimilars into **pharmacy benefit** reimbursement
- Biosimilars in **more classes**
- Approval of **interchangeable biosimilars** in the US



Current US regulatory standards for developing and approving biosimilars, as well as for establishing interchangeability, are **scientifically appropriate to protect patient safety and support provider and payer confidence**. It is important to maintain these appropriate standards to support a sustainable biosimilars marketplace.



Essential components of provider and patient use of biosimilars include **addressing the clinical, economic, and operational considerations relevant to adoption as well as payer coverage**.



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 clinical, economic, and operational decision-making drivers of providers and payers**.



Competitive mechanisms are in place to support biosimilar uptake. For example, the Centers for Medicare & Medicaid Services (CMS) has established separate Healthcare Common Procedure Coding System (HCPCS) **codes and payment rates for biosimilars, treating them similarly to other biologics, which supports their uptake and can help lead to meaningful cost savings and a sustainable marketplace**. Additionally, Medicare reimburses for biosimilars at their ASP plus a 6% add-on of the reference biologic's ASP.<sup>7</sup>

### INTRODUCTION AND REPORT OVERVIEW

Foreword: A Word From Our VP of US Value and Access

About Amgen

2021 Biosimilar Trends Report Key Takeaways

### CURRENT STATE OF THE MARKETPLACE

### FUTURE STATE OF THE MARKETPLACE

### TRENDS

### STAKEHOLDER CONSIDERATIONS

### REIMBURSEMENT

### POLICY UPDATE

### UNDERSTANDING BIOSIMILARS

### REFERENCES



# CURRENT STATE OF THE MARKETPLACE

- Trends in US Biosimilar Approvals and Launches
- Timeline of Approved Biosimilars and Launch Dates
- Trends in ASP, Uptake, and Total Drug Spend
- Boxed Warnings for Amgen Products

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



# CURRENT STATE OF THE MARKETPLACE



The US marketplace is poised to see further growth in biosimilars approved to date and welcome many new biosimilars in the years to come, spurring additional competition that will potentially lead to significant savings for the healthcare system, which can then be deployed to newer, innovative treatments.<sup>6</sup>

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

Essential components of provider and patient use of biosimilars include addressing the clinical, operational, and economic considerations to help support adoption as well as payer coverage.

Biosimilar adoption is only one of many measures of a successful marketplace. Reference products frequently lower prices to compete, which is a positive outcome that results from biosimilar competition.<sup>8</sup>

While financial savings are important for helping support 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, operational, and decision-making drivers.

**“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.”<sup>9</sup>**

– Sean McGowan  
Senior Director of Biosimilars, AmerisourceBergen

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES





# US BIOSIMILAR APPROVALS AND LAUNCHES, 7-YEAR TREND

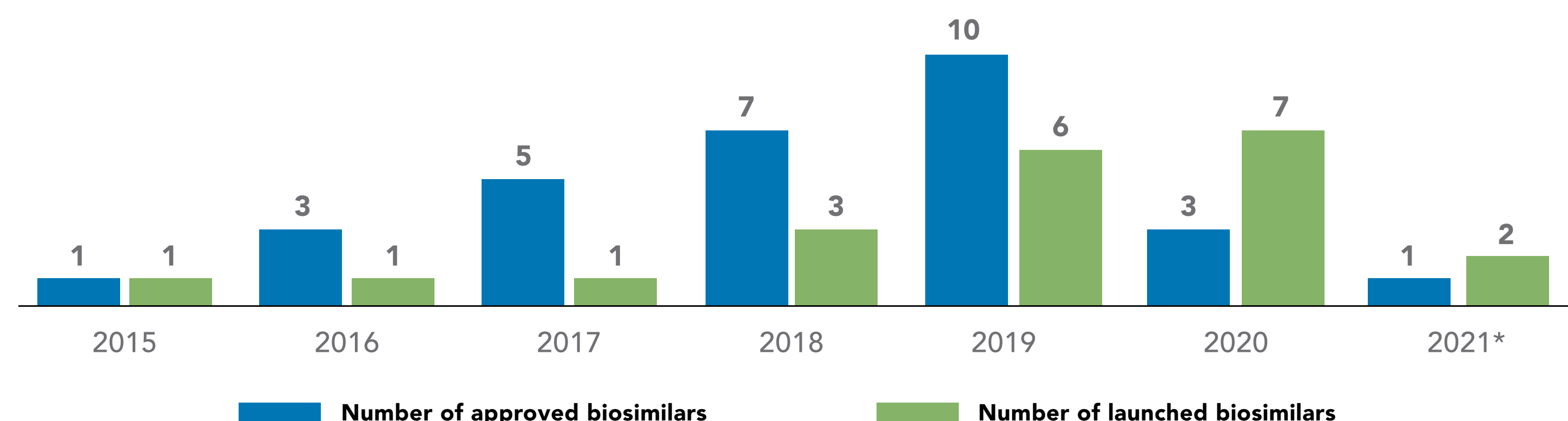
The US marketplace for biosimilars is now well-established and accelerating across multiple therapeutic areas. **Figure 1** shows the number of biosimilars approved and launched each year from 2015 to 2021. There was a dramatic increase in biosimilar launches in 2019 and 2020 compared to prior years. <sup>1</sup>

The slowdown of biosimilar approvals in 2020 and thus far in 2021 was likely due to several pandemic-related factors including clinical trial delays and a shift in the FDA's resources toward managing trials and reviews for COVID-19 vaccine candidates and related therapies.

By the end of 2018, there were only **6 biosimilars** available.

In 2019, **6 more biosimilars** became available, followed by another **7** in 2020.

**Figure 1.** Number of Approved and Launched Biosimilars in the US, per Year <sup>1</sup>



**30** Total number of approved biosimilars

**21** Total number of launched biosimilars

Although the number of approvals declined in 2020, the number of development programs that are participating in the FDA's Biosimilar Development Program per year has continued to rise <sup>10</sup>:

**64 programs**  
in March 2018

**77 programs**  
in March 2019

**79 programs**  
in March 2020

**90 programs**  
in March 2021

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

FUTURE STATE OF THE MARKETPLACE

TRENDS

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# US BIOSIMILAR APPROVALS COMPARED TO THE EU

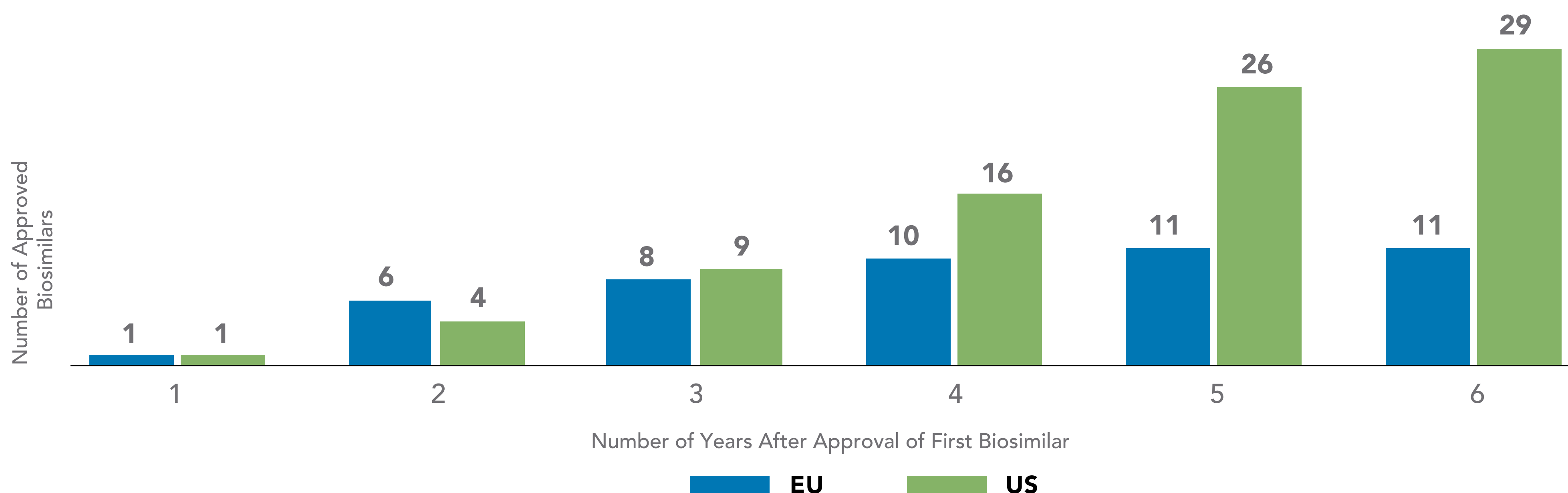
Current data support that the US biosimilar landscape is advancing faster than the EU biosimilar landscape during a comparable period of time.

**Figure 2** shows the cumulative number of biosimilars approved in the EU vs the US, beginning with the year the first biosimilar was approved. <sup>1</sup>

**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 (2015), there were 29 approved biosimilars.**

**Figure 2.** Comparison of Approved Biosimilars in the EU and the US <sup>12,13</sup>



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

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

FUTURE STATE OF THE MARKETPLACE

TRENDS

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

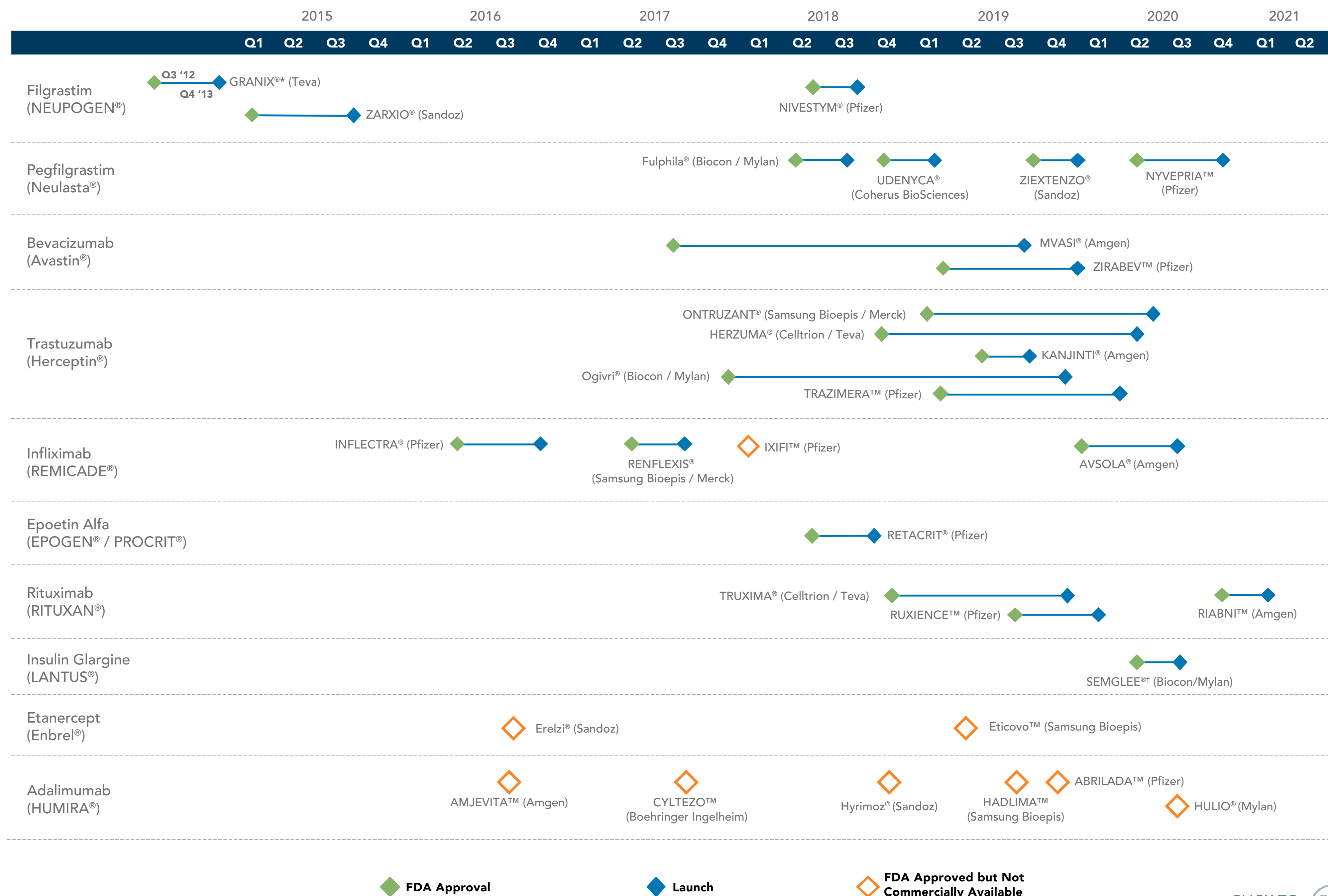
UNDERSTANDING BIOSIMILARS

REFERENCES

# TIMELINE OF APPROVED BIOSIMILARS AND LAUNCH DATE

As of July 2021, the FDA has approved 30 biosimilars and 21 biosimilars have been launched in the US as shown in **Figure 3**. Currently, there are 10 reference products that have approved biosimilars.

**Figure 3.** Approved and Launched Biosimilars (including GRANIX\*) in the US<sup>1</sup>



Please [click here](#) for Boxed Warning information for AVSOLA, EPOGEN, Enbrel, KANJINTI, and RIABNI.

Key: BLA – Biologics License Application; FDA – Food and Drug Administration; US – United States.  
 \*GRANIX is not a biosimilar. It was approved under a stand-alone BLA, which was submitted to the FDA before the enactment of the biosimilar approval pathway.  
 †SEMGLEE was approved by the FDA in June 2020 with a stand-alone BLA. The FDA subsequently approved SEMGLEE as an interchangeable biosimilar in July 2021.<sup>11</sup>

CLICK TO ENLARGE

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
  - Trends in US Biosimilar Approvals and Launches
  - Timeline of Approved Biosimilars and Launch Dates
  - Trends in ASP, Uptake, and Total Drug Spend
  - Boxed Warnings for Amgen Products
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# BIOSIMILARS LAUNCH WITH SIGNIFICANT DISCOUNTS TO WAC AND ASP

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

As shown in **Figure 4**, manufacturers are launching biosimilars at a WAC that is generally lower than the reference product (biosimilars' ASP becomes available 2 full quarters after launch).<sup>14</sup>

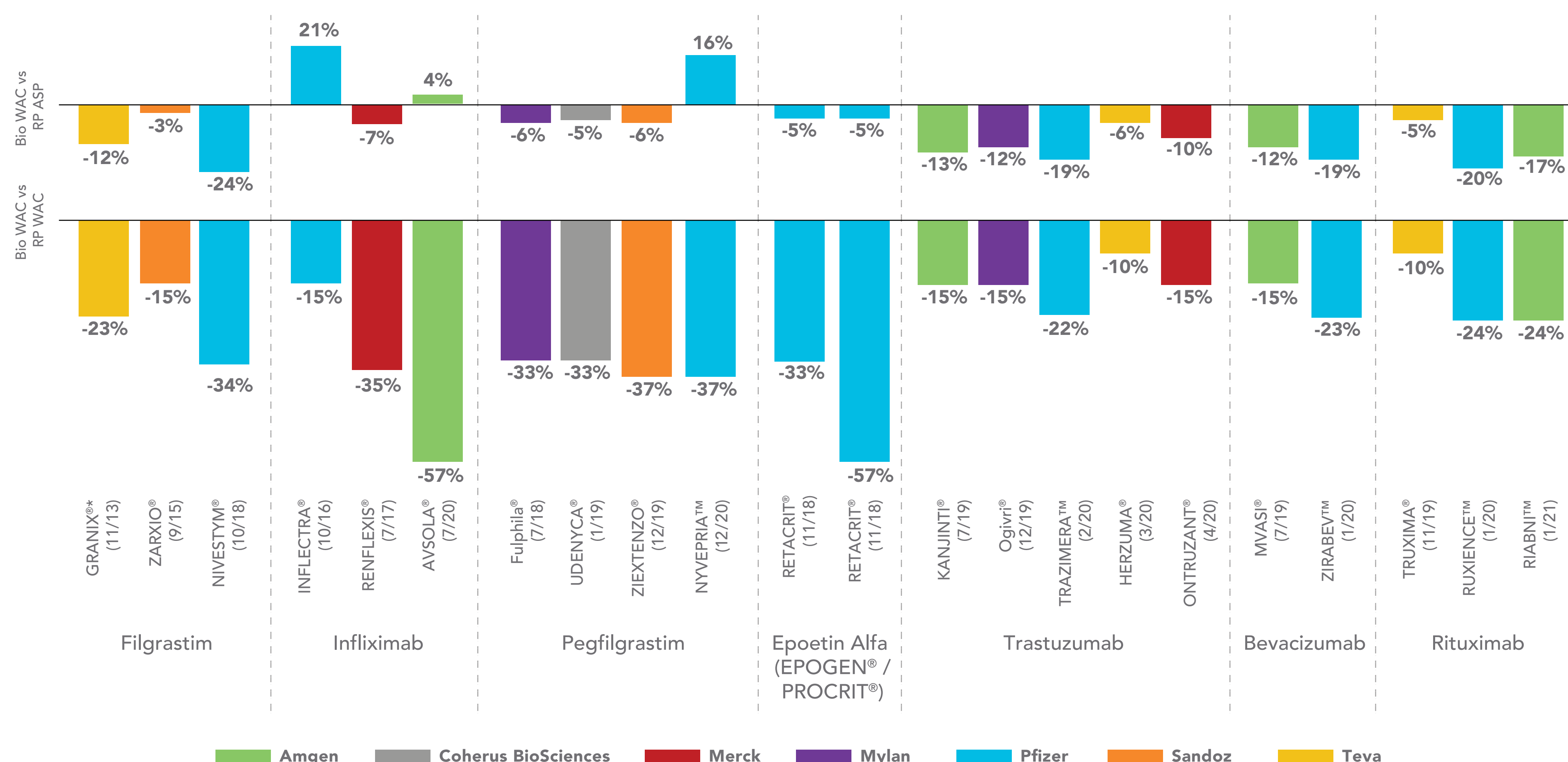
*Biosimilar WAC vs Reference Product ASP:*

**Almost all biosimilars have launched at a WAC 3% to 24% below the reference product ASP.**

*Biosimilar WAC vs Reference Product WAC:*

**Biosimilars launch at a WAC that is generally 15% to 37% lower than the reference product.**

**Figure 4. Price at Launch vs Reference Product<sup>2</sup>**



Please [click here](#) for Boxed Warning information for AVSOLA, EPOGEN, Enbrel, KANJINTI, and RIABNI.

Key: ASP – average sales price; Bio – biosimilar; FDA – Food and Drug Administration; RP – reference product; WAC – wholesale acquisition cost.  
 \*GRANIX is not a biosimilar. It was approved under a stand-alone Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.  
 Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

FUTURE STATE OF THE MARKETPLACE

TRENDS

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

CLICK TO ENLARGE

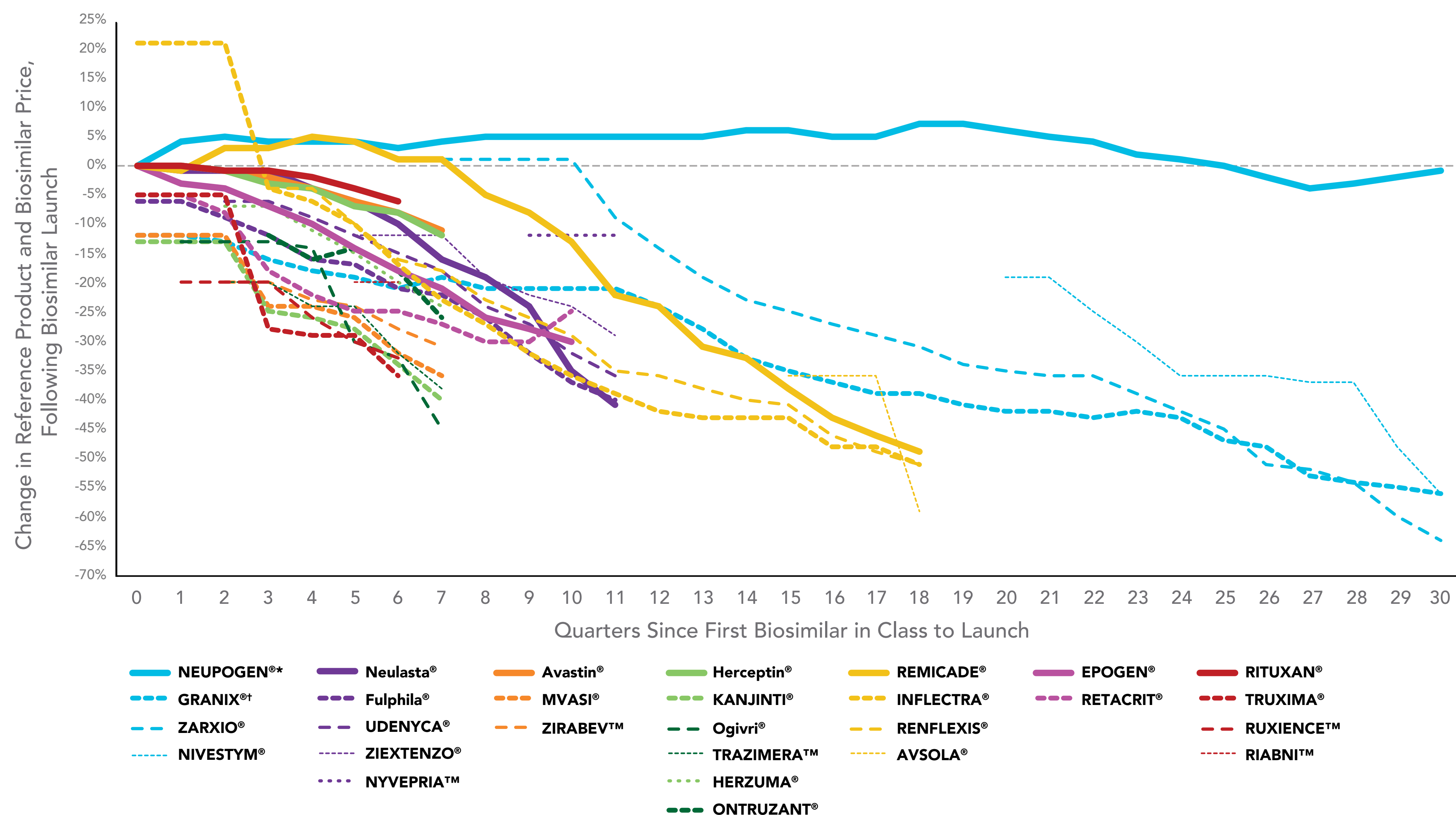
# ASPs ARE DECLINING FOR BOTH REFERENCE AND BIOSIMILAR PRODUCTS

As expected, competition usually results in lower ASP for both reference products and biosimilars, leading to additional savings. As shown in **Figure 5**, in most cases, the prices of biosimilars decline once ASP is established and continue a steady downward trend. The ASPs for reference products are also declining over time, leading to further opportunity for healthcare savings.

The prices of biosimilars are decreasing at a CAGR of 9% to 19%.

The prices of most reference products\* are decreasing at a CAGR of 4% to 17%.

**Figure 5.** Downward Trend in ASP for Biosimilars and Reference Products Over Time<sup>2</sup>



Please [click here](#) for Boxed Warning information for AVSOLA, EPOGEN, Enbrel, KANJINTI, and RIABNI.

Key: ASP – average sales price; CAGR – compound annual growth rate; FDA – Food and Drug Administration.  
 \*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.  
 †GRANIX is not a biosimilar. It was approved under a stand-alone Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.  
 Source: AnalySource.

CLICK TO ENLARGE

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
  - Trends in US Biosimilar Approvals and Launches
  - Timeline of Approved Biosimilars and Launch Dates
  - Trends in ASP, Uptake, and Total Drug Spend
  - Boxed Warnings for Amgen Products
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# BIOSIMILAR UPTAKE IS ACCELERATING

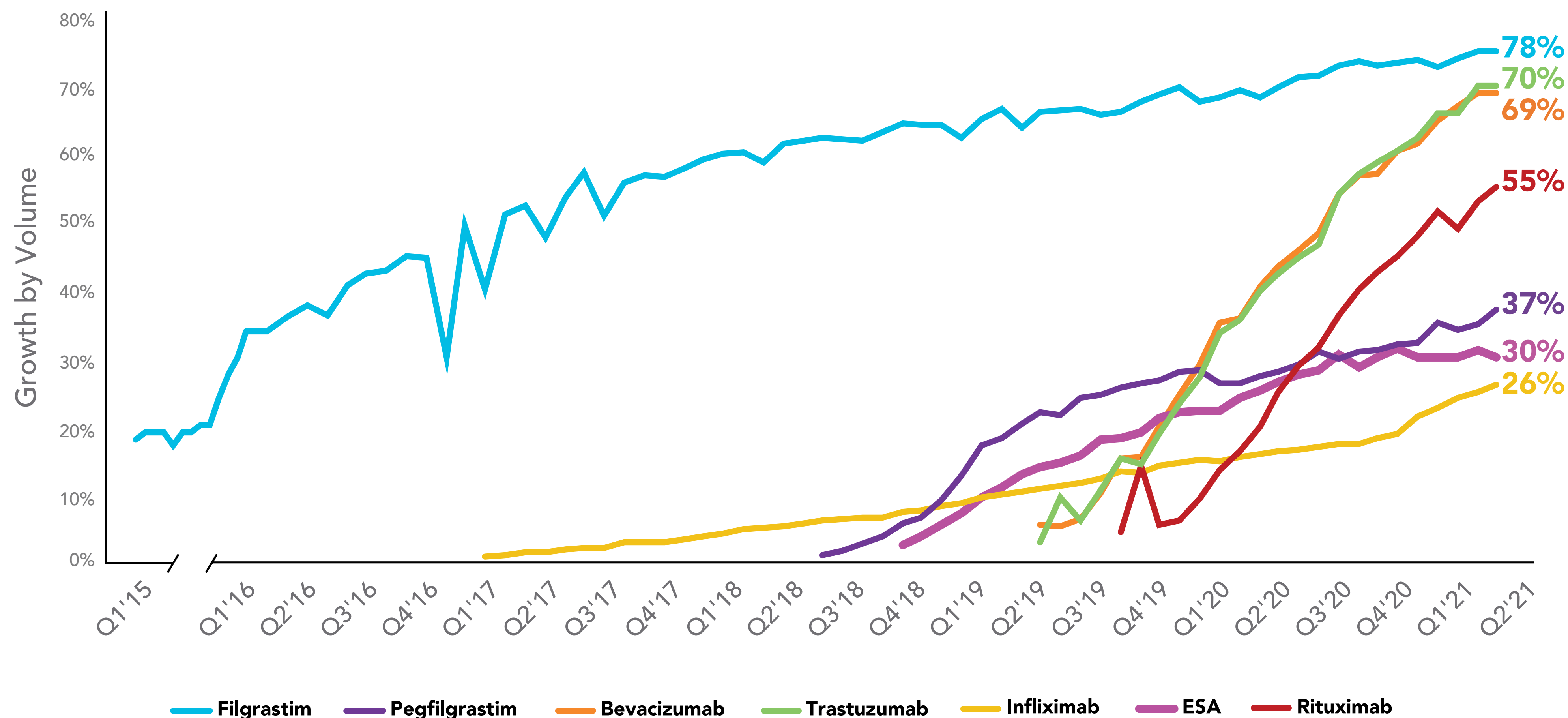


The rate of biosimilar uptake is generally increasing over time, as depicted in **Figure 6**. Biosimilars have gained significant share in the majority of therapeutic areas where they have been introduced. Additionally, first-to-launch biosimilars tend to capture a greater portion of the segment compared to later entrants.

**For therapeutic areas with biosimilars launched in the last 2 years, the average share was 65%.**

**For therapeutic areas with biosimilars launched prior to 2019, the average share after 2 years was 13%.**

**Figure 6. Biosimilars Uptake Curve**<sup>5</sup>



- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
  - Trends in US Biosimilar Approvals and Launches
  - Timeline of Approved Biosimilars and Launch Dates
  - Trends in ASP, Uptake, and Total Drug Spend
  - Boxed Warnings for Amgen Products
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

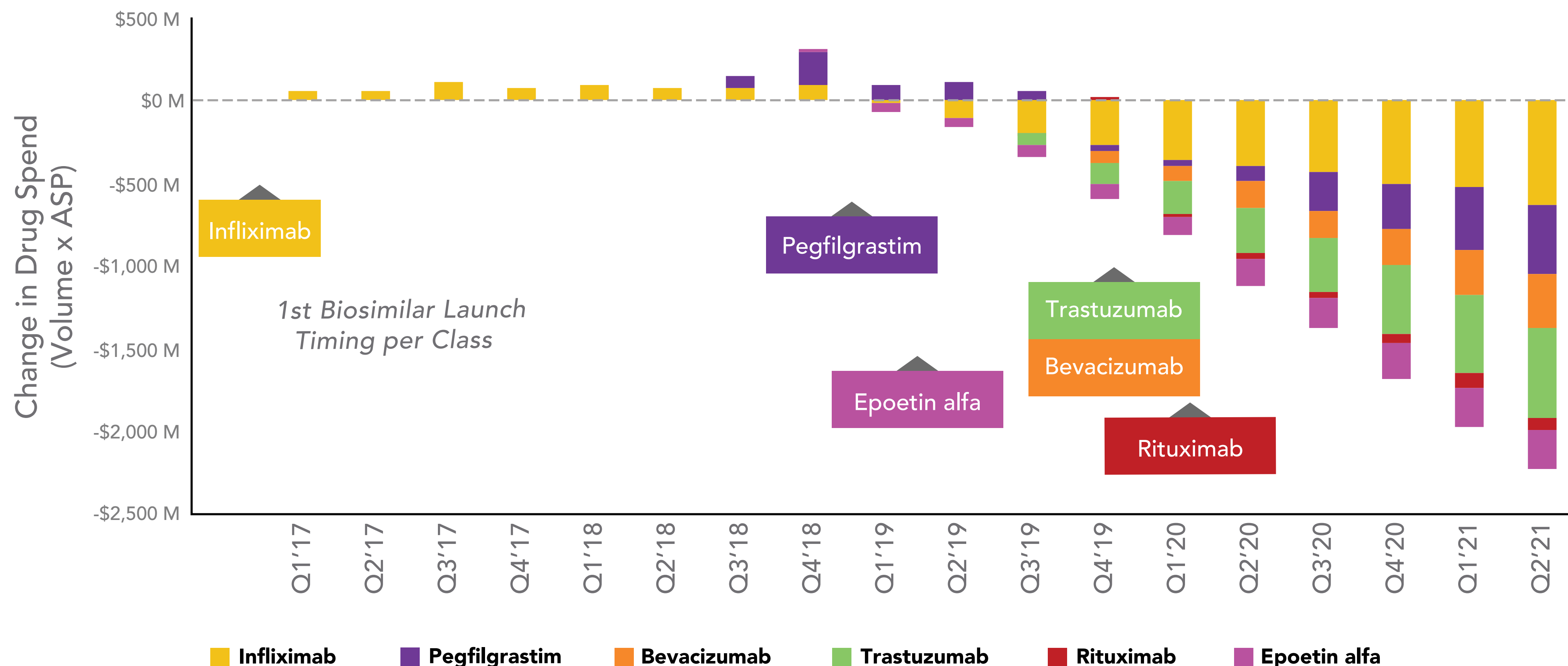
Key: ESA – erythropoiesis-stimulating agent.  
Source: OBU Customer Data Pack Weekly (IQVIA DDD + Chargeback).

# BIOSIMILAR COMPETITION APPEARS TO BE CONTRIBUTING TO DECREASED DRUG SPENDING

**Figure 7** shows the estimated decrease in total drug spend after biosimilar competition was introduced. Change in drug spend shown is the delta between the projected reference product spend (based on historical trend) vs the actual spend following biosimilar launch. Beginning in Q1 2019, the estimated change in drug spending for most classes continued to decrease.

The cumulative savings in drug spend for classes with biosimilar competition is estimated to have been **\$9.8 billion** over the past 5 years.

**Figure 7. Estimated Change in Total Drug Spend After Biosimilar Competition<sup>3</sup>**



Key: ASP – average sales price.

Note: Filgrastim is excluded from figure because the first biosimilar in its class was launched in 2013 and data are not available prior to Q2 2016 for normalized units.

The quarterly drug spend for each product is estimated as: Drug spend=ASPxNormalized unit volume. The estimated spend for the reference product (after biosimilar launch) is trended out based on historical spend for the reference product before biosimilar launch.

Sources: AnalySource, Integrated Weekly Sales Data (IQVIA DDD + Chargeback).

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

FUTURE STATE OF THE MARKETPLACE

TRENDS

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES



# BOXED WARNINGS FOR AMGEN PRODUCTS

## 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 (2.2).
- 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).

## 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)

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



# BOXED WARNINGS FOR AMGEN PRODUCTS

## 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)

## 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)

## 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).

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

Trends in US Biosimilar Approvals and Launches

Timeline of Approved Biosimilars and Launch Dates

Trends in ASP, Uptake, and Total Drug Spend

Boxed Warnings for Amgen Products

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



# FUTURE STATE OF THE MARKETPLACE

- The Future of Biosimilars in the US
- The Future of Autoimmune Therapies
- Lessons for the Future From Real-World Evidence
- Important Considerations for the Future

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

Lessons for the Future From Real-World Evidence

Important Considerations for the Future

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

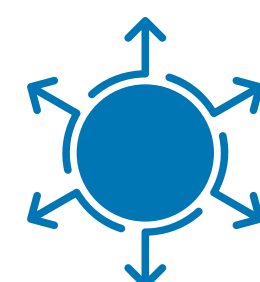


# THE FUTURE OF BIOSIMILARS IN THE US

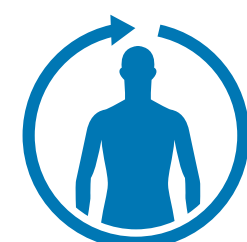
## Biosimilars are expanding into new areas

We expect growth in the number of biosimilars, both in terms of breadth and depth. As of Q2 2021, the FDA lists 90 proposed biosimilar products enrolled in the FDA's Biosimilar Development Program, an almost 60% increase since October 2015.<sup>10</sup>

**This growing number of biosimilars will likely lead to a rapid evolution in the US biosimilars marketplace. Over the next few years, we expect to see several advancements, including:**



Expansion of biosimilars into pharmacy benefit reimbursement



Biosimilars in more therapeutic areas



Approval of additional interchangeable biosimilars in the US

These changes are likely to cement the role of biosimilars as viable and integral US treatment options. Biosimilars will find new audiences in different prescriber specialties, pharmacists, payers, and patients. These developments may change the patient support program landscape, interactions at the pharmacy counter, and product-administration devices.

New biosimilars are expected in multiple therapeutic areas, including immune-mediated inflammatory (ie, autoimmune) diseases, oncology, and endocrinology. Some of the best-selling biologics are expected to have biosimilar competition in the next few years, such as LUCENTIS® (ranibizumab), HUMIRA® (adalimumab), STELARA® (ustekinumab), CIMZIA® (certolizumab pegol), and Prolia®/XGEVA® (denosumab).

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● **FUTURE STATE OF THE MARKETPLACE**

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

Lessons for the Future From Real-World Evidence

Important Considerations for the Future

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

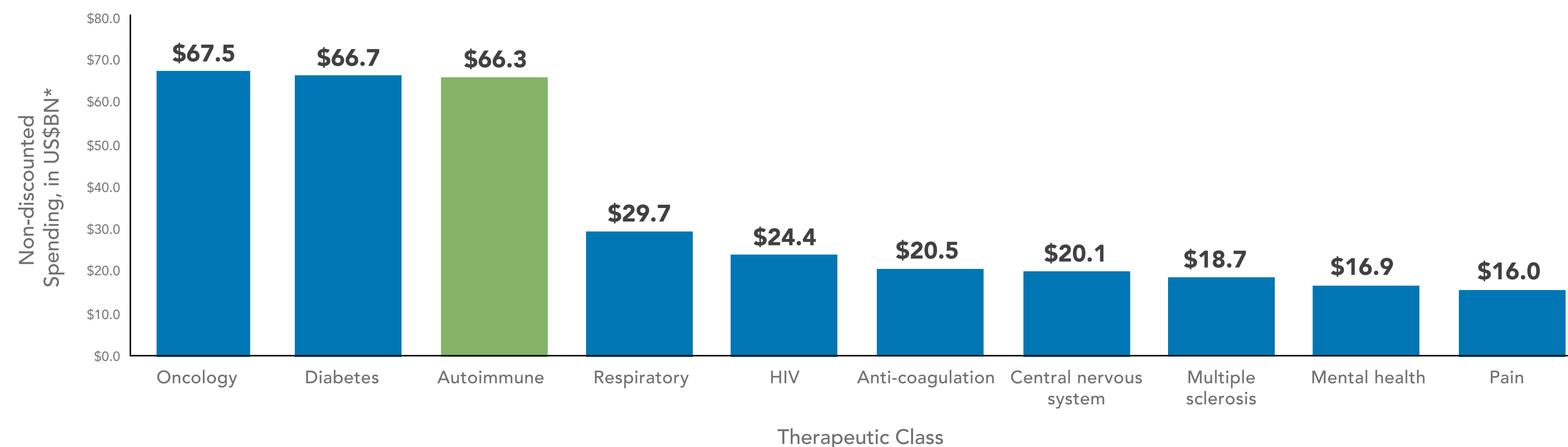


# THE FUTURE OF AUTOIMMUNE THERAPIES

## Autoimmune therapies are the third largest therapeutic class by spend

While there is a new wave of biosimilar competition expected across several therapeutic areas, anticipated entrants in the autoimmune space have the potential to significantly impact the landscape within the next 2 to 3 years. As shown in **Figure 8**, drugs treating autoimmune conditions are the third largest therapeutic area by non-discounted drug spend, only slightly trailing oncology and diabetes.<sup>15</sup>

**Figure 8.** Top Therapeutic Classes by Non-Discounted Spending in 2019 (Billions)<sup>15</sup>



● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

Lessons for the Future From Real-World Evidence

Important Considerations for the Future

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

\*It is common for manufacturers to offer rebates or discounts that may impact the actual costs of medicines. These figures represent spending prior to any rebates or discounts.

# THE FUTURE OF AUTOIMMUNE THERAPIES

## HUMIRA® (adalimumab), the top-selling drug in the world, makes up nearly a third of autoimmune sales

As shown in **Table 1**, sales of HUMIRA in 2020 (\$20.4 billion) were almost 160% higher than the next closest autoimmune biologic, STELARA (ustekinumab).<sup>16</sup>

Within the autoimmune area, the planned launches of biosimilars to HUMIRA in 2023 could be a pivotal moment. HUMIRA has the highest number of anticipated biosimilar launches in the US over the next few years, when compared to reference products in other categories.

**Table 1. Top-Selling Autoimmune Drugs in 2020**<sup>16-19</sup>

Product	Manufacturer	2020 global sales (billions)
<b>HUMIRA (adalimumab)</b>	AbbVie	\$20.4
<b>STELARA (ustekinumab)</b>	Janssen	\$7.9
<b>Enbrel (etanercept)</b>	Amgen	\$6.4
<b>REMICADE (infliximab)</b>	Janssen	\$4.2

Please [click here](#) for Boxed Warning information for Enbrel.

As shown in **Table 2**, there are currently 6 FDA-approved biosimilars for the reference product HUMIRA, with the possibility of 8 or more launches in 2023. HUMIRA treats a range of conditions across gastroenterology, rheumatology, and dermatology, and biosimilars are expected to be granted approval for all HUMIRA indications. The resulting competition could generate significant savings for payers, employers, and patients. Based on the history of pricing for biosimilar and reference products seen in other areas, the entry of additional biosimilars is expected to lead to greater price declines across all products within the class.

**Table 2. Launch Dates of Biosimilars to HUMIRA as Agreed in Settlements With HUMIRA Manufacturer AbbVie**<sup>1,13,20,21</sup>

Company	Drug	FDA approved	Anticipated US launch*	Launched in the EU
Amgen	AMJEVITA <sup>†</sup>	☑	January 31, 2023	☑
Samsung Bioepis/Merck	HADLIMA <sup>‡</sup>	☑	June 30, 2023	☑
Boehringer Ingelheim	CYLTEZO	☑	July 1, 2023	☑
Mylan	HULIO	☑	July 31, 2023	☑
Sandoz	Hyrimoz	☑	September 30, 2023	☑
Pfizer	ABRILADA	☑	November 20, 2023	
Fresenius Kabi	IDACIO		September 30, 2023	☑
Coherus BioSciences	CHS-1420		December 15, 2023	
Celltrion <sup>§</sup>	Yuflyma		N/A	
Alvotech <sup>#</sup>	AVT02		N/A	

Data current as of Q3 2021.

Key: EU – European Union; FDA – Food and Drug Administration; US – United States.

\*Companies may launch earlier than their settlement date.

<sup>†</sup>AMJEVITA is marketed as AMGEVITA in the EU.

<sup>‡</sup>HADLIMA is marketed as IMRALDI in the EU and manufactured/marketed by Samsung Bioepis/Biogen.

<sup>§</sup>Celltrion announced it completed patent settlements in the US but the anticipated launch date is not public.

<sup>#</sup>At time of publication, Alvotech had not signed a licensing deal with AbbVie.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

Lessons for the Future From Real-World Evidence

Important Considerations for the Future

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

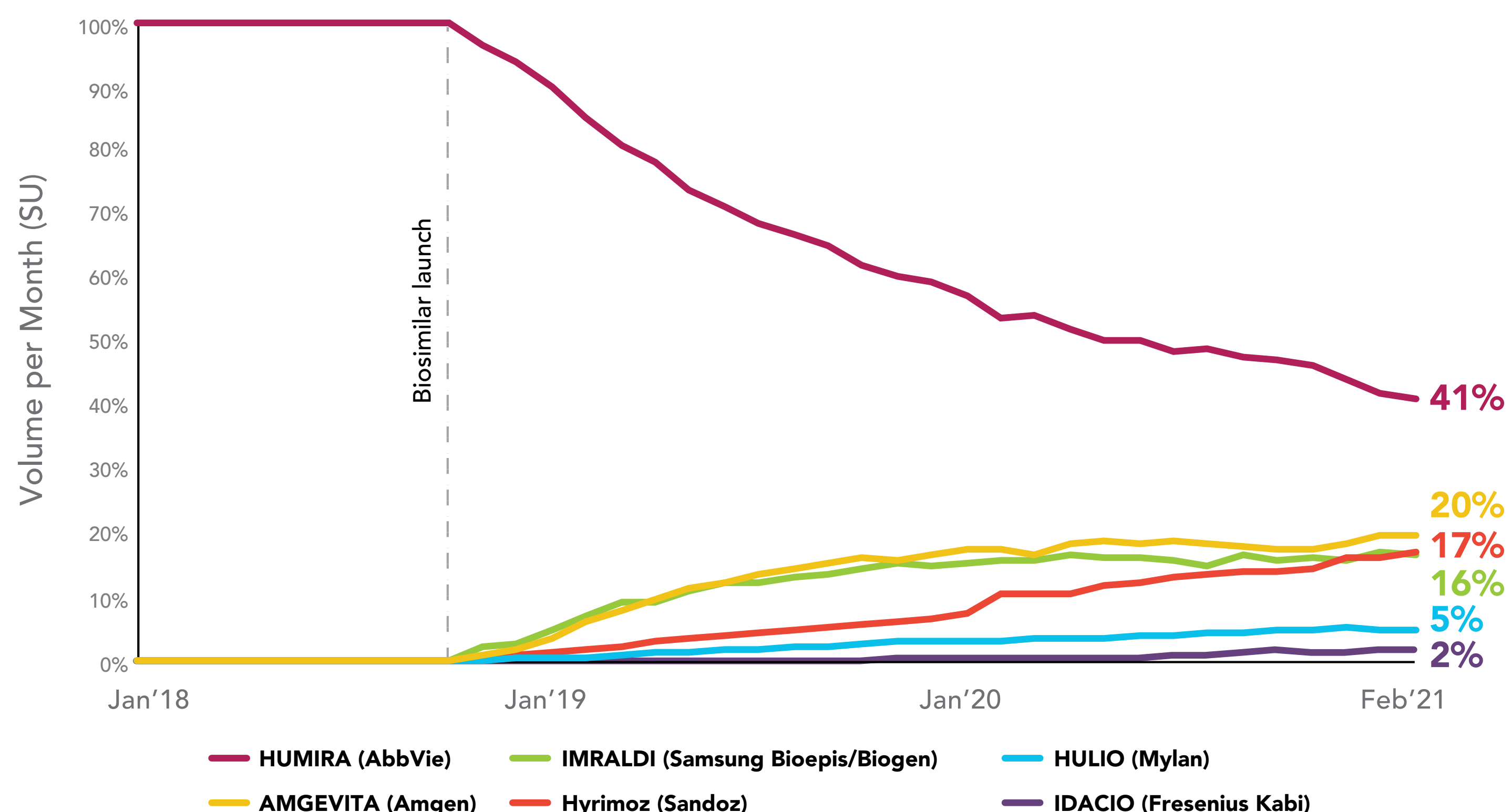


# LESSONS FOR THE FUTURE FROM REAL-WORLD EVIDENCE

## Uptake of biosimilars to HUMIRA (adalimumab) in the EU has been steady since 2019

As shown in **Figure 9**, HUMIRA's share has declined in the EU since the introduction of biosimilar competition. At the time of publication, HUMIRA had a 41% share, while AMGEVITA – the first biosimilar in the market – had a 20% share, followed by Hyrimoz (17%) and IMRALDI (16%).<sup>22</sup>

**Figure 9.** Adalimumab Volume Analysis in the EU<sup>22</sup>



Adoption of adalimumab biosimilars is higher in some EU countries due to varying healthcare systems and government policies. For example, the AMGEVITA share differs by country, with

- 40% share in the UK
- 21% share in Germany
- 17% share in France<sup>22</sup>



**Key Takeaway: Uptake of biosimilars to HUMIRA in the EU has been strong, and biosimilar products now make up nearly 60% of the adalimumab share.**

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

Lessons for the Future From Real-World Evidence

Important Considerations for the Future

TRENDS

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# LESSONS FOR THE FUTURE FROM REAL-WORLD EVIDENCE

## Physician comfort with prescribing autoimmune biosimilars in the EU

Data on biosimilars in the real-world setting are increasing as clinical experience with biosimilars to treat autoimmune conditions such as inflammatory bowel disease, psoriasis, and rheumatoid arthritis grows. Studies using real-world evidence (RWE) from the EU help support the effectiveness, safety, and tolerability of biosimilars in patients.

*Findings from an analysis of several recent RWE studies on autoimmune biosimilars in the EU:*



Results are largely consistent with the evidence from randomized controlled trials<sup>23-25</sup>



In RWE studies, biosimilars show similar effectiveness and safety to the reference product<sup>26</sup>



Outcomes were generally consistent regardless of whether patients were biologic-naïve or switched from another biologic<sup>23</sup>

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● **FUTURE STATE OF THE MARKETPLACE**

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

[Lessons for the Future From Real-World Evidence](#)

Important Considerations for the Future

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

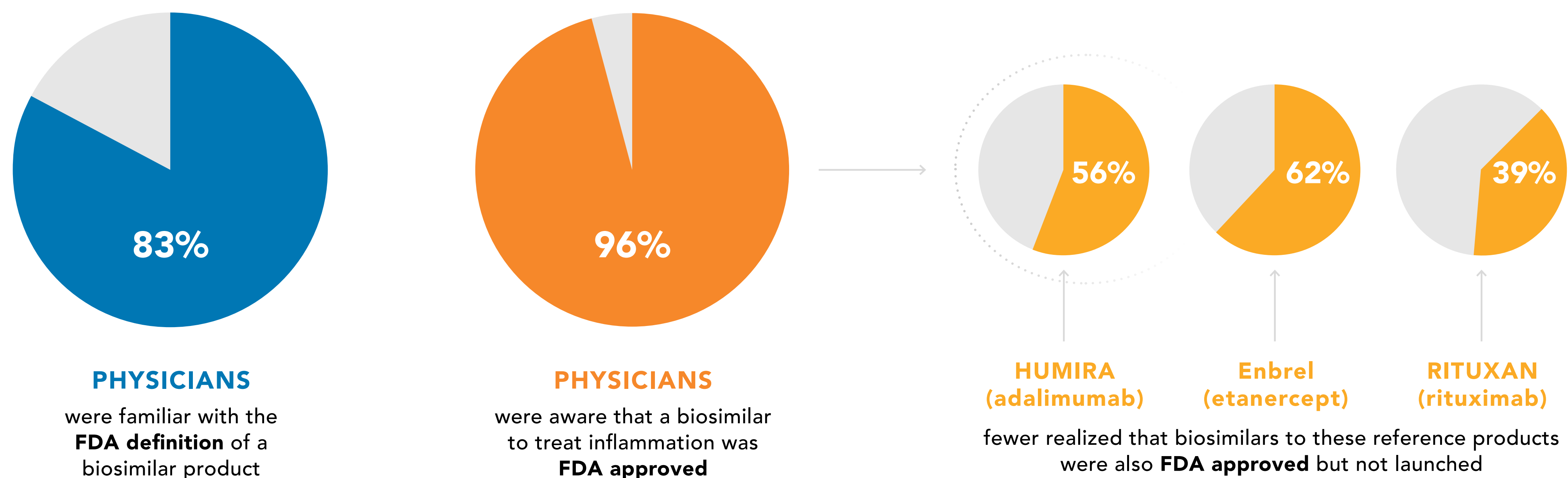
# LESSONS FOR THE FUTURE FROM REAL-WORLD EVIDENCE

## Physicians' attitudes about prescribing autoimmune biosimilars in the US

Although physician perspectives about prescribing biosimilars to HUMIRA are not widely available in the US because the products are not yet on the market, there are recent data about physician prescribing preferences for other autoimmune biosimilars on the market.

In 2021, WebMD published a survey of 320 board-certified US rheumatologists regarding their perceptions of biosimilar products.<sup>27</sup> As shown in **Figure 10**, 83% were familiar with the FDA definition of a biosimilar product and 96% were aware that a biosimilar to treat inflammation was FDA approved; however, fewer realized that biosimilars to HUMIRA (adalimumab) (56%), Enbrel (etanercept) (62%), and RITUXAN (rituximab) (39%) were also FDA approved but not launched. Rheumatologists were more likely to initiate biosimilar treatment for a biologic treatment-naïve patient with rheumatoid arthritis (73%) than they were to switch to a biosimilar for a patient with rheumatoid arthritis doing well on the reference product (35%).

**Figure 10.** Physician Familiarity With Autoimmune Biosimilars<sup>27</sup>



Please [click here](#) for Boxed Warning information for Enbrel.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

**FUTURE STATE OF THE MARKETPLACE**

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

Lessons for the Future From Real-World Evidence

Important Considerations for the Future

TRENDS

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES





# IMPORTANT CONSIDERATIONS FOR THE FUTURE

## Stakeholder considerations



### Payers/PBMs

- Payers and PBMs often put greater emphasis on cost minimization, when outcomes are equal or assumed to be equal<sup>28</sup>
- Their concern is typically on balancing risk and ensuring that premiums are low enough to attract/retain members while providing adequate access to benefits
- Non-cost differentiators such as product portfolio, category experience, and the ability to pull through coverage decisions may resonate here



### Employers

- Escalating specialty drug costs present a challenge for employers trying to provide healthcare for their employees
- Employers are uniquely motivated to ensure continued health and productivity while considering cost-effectiveness
- Greater biosimilar market penetration could help to lower drug plan costs without compromising quality, efficacy, or patient safety
- While specialty drug costs are important, patient support programs to help patients initiate and adhere to therapy should also be considered



### Pharmacists

- To date, there are 21 biosimilars on the market – however, none of the launched biosimilars are routinely processed through the pharmacy benefit. The launch of biosimilars that are processed under the pharmacy benefit will probably be the first time many pharmacists are introduced to them
- As of July 2021, 1 biosimilar with an interchangeable designation is approved in the US.<sup>11</sup> All 50 states plus Puerto Rico and DC allow pharmacists to substitute a prescribed reference product with an approved, interchangeable biosimilar, consistent with state law<sup>29</sup>
- Public information is [available](#) to assist pharmacists in evaluating biosimilars for formulary inclusion
- Pharmacists will likely need substantial education to become knowledgeable and comfortable discussing biosimilars with patients. Educational outreach will be another opportunity for an experienced manufacturer to become a trusted partner

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

The Future of Biosimilars in the US

The Future of Autoimmune Therapies

Lessons for the Future From Real-World Evidence

Important Considerations for the Future

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



# TRENDS

- > Oncology Therapeutics
- > Oncology Supportive Care
- > Nephrology/Oncology Supportive Care
- > Inflammation

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● **TRENDS**

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



# ONCOLOGY THERAPEUTICS



The biosimilars available for oncology therapeutics consist of **trastuzumab**, **bevacizumab**, and **rituximab** products. For each, we discuss:

- 1 WAC and ASP of the biosimilar at launch compared to the reference product**
- 2 ASP for the reference product and biosimilars since launch**
- 3 Biosimilar uptake**
- 4 Estimated difference in total drug spend after biosimilar competition**

Biologics account for half of the pharmacological products in oncology; however, their high cost is a result of greater costs of development and production compared to small molecules.<sup>30</sup> Biosimilars can help drive down that high cost with 14 becoming available to patients from 2019 to 2021 (as of July).<sup>1</sup>

As this section demonstrates, biosimilars available for oncology therapeutics have exhibited strong growth. For example, both trastuzumab and bevacizumab biosimilars account for nearly 70% of sales by volume. The rituximab biosimilars are comparatively newer, though they still account for 55% of sales by volume.<sup>5</sup>

**“We have to address the problem of cancer drug costs, and biosimilars may help us.”<sup>31</sup>**

– Sara Hurvitz, MD  
Associate Professor at the David Geffen School of Medicine at UCLA;  
Medical Director of the Jonsson Comprehensive Cancer Center Clinical Research Unit;  
Co-director of the Santa Monica-UCLA Outpatient Oncology Practices;  
Director of the Breast Cancer Clinical Trials Program at UCLA

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

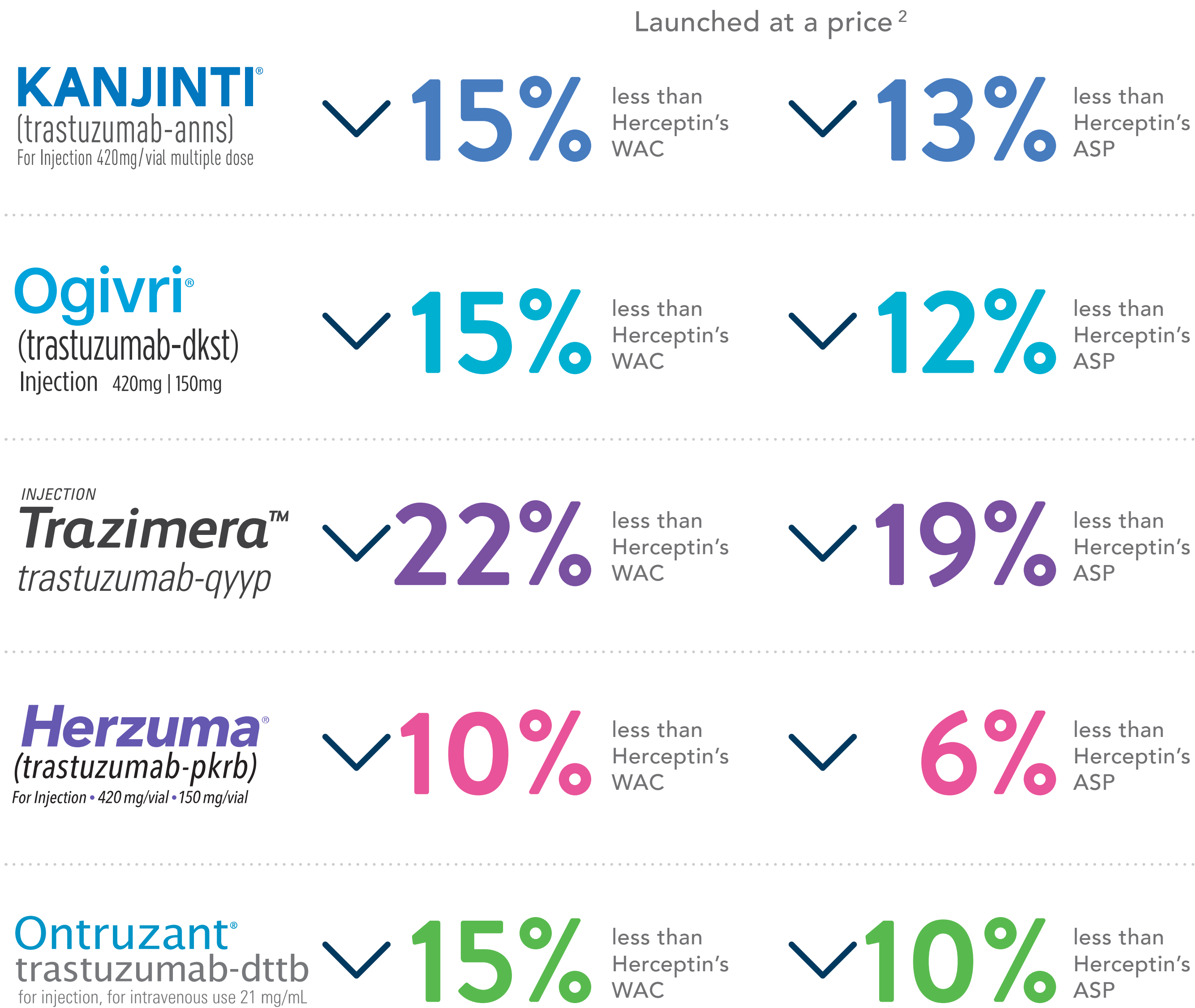
● REFERENCES



# ONCOLOGY THERAPEUTICS

## Trastuzumab

Five biosimilars have launched since 2019 to the reference product Herceptin (trastuzumab):



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- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

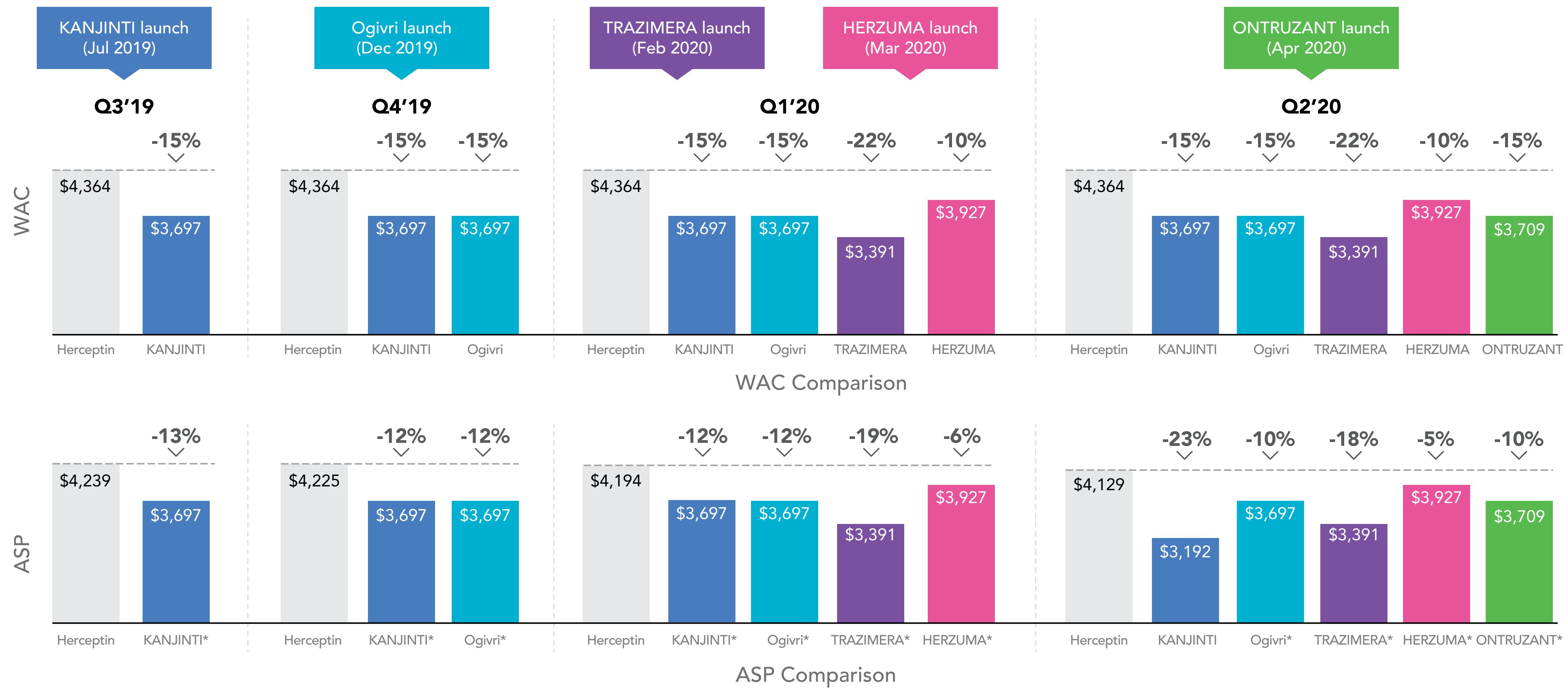
# ONCOLOGY THERAPEUTICS



## Trastuzumab

As **Figure 11** shows, all 5 biosimilars launched at WAC and ASP discounts to the reference product with some launching at discounts below their predecessors.

**Figure 11.** WAC and ASP of Trastuzumab Biosimilars Relative to Reference Product at Launch<sup>2</sup>



Please [click here](#) for Boxed Warning information for KANJINTI.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
\*ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
Source: AnalySource.

CLICK TO ENLARGE

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# ONCOLOGY THERAPEUTICS

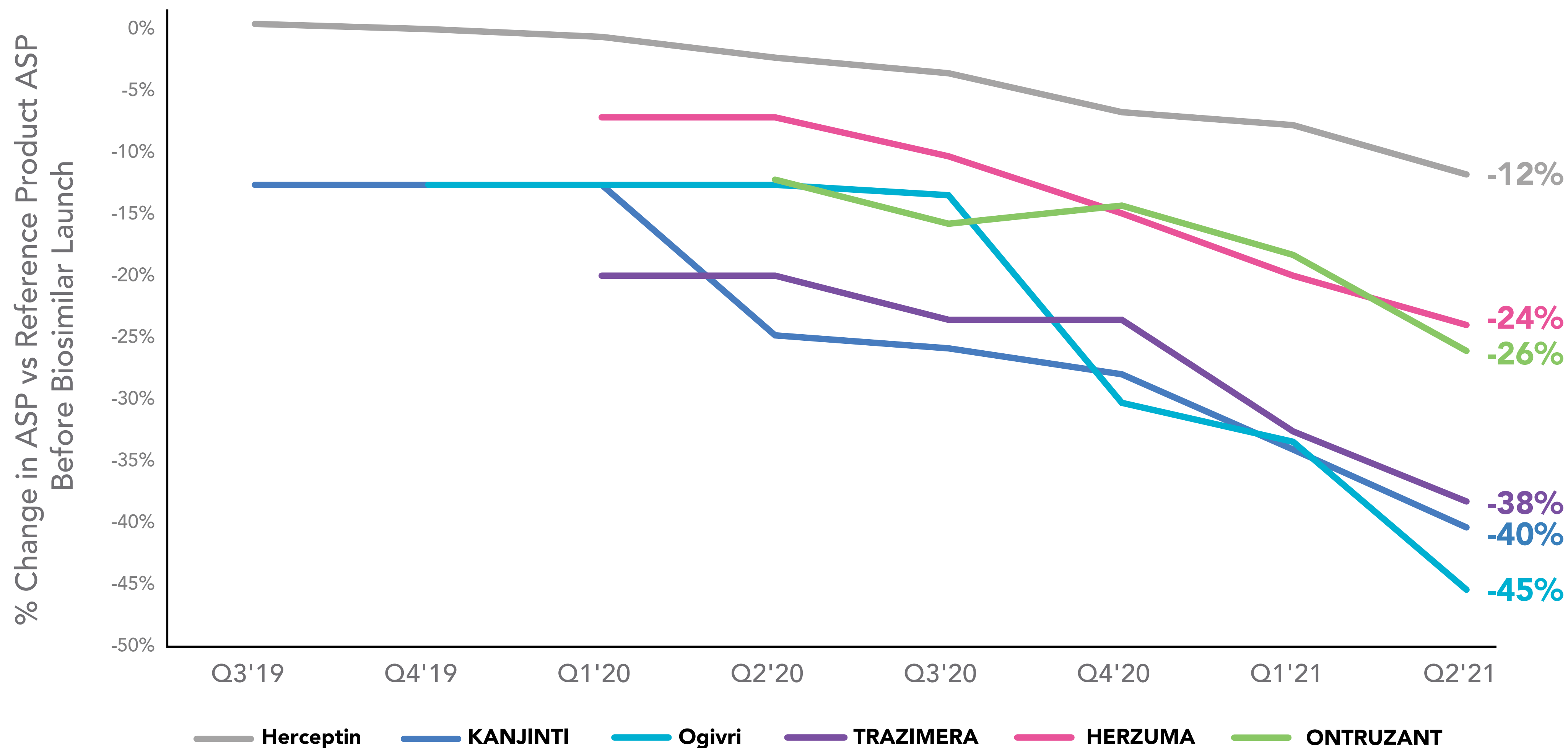


## Trastuzumab

**Figure 12** shows the percentage change in the price of biosimilars over time when compared to the reference product's ASP at the time that the first trastuzumab biosimilar launched.

**While the prices of all trastuzumab products have declined over time, biosimilar prices are now 24% to 45% lower than the reference product Herceptin's ASP at the time of the first biosimilar launch.**

**Figure 12.** ASP of Trastuzumab Products at Biosimilars' Launches<sup>2</sup>



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See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
 Biosimilar WAC is used for comparing against reference product ASP until biosimilar ASP is available.  
 Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY THERAPEUTICS

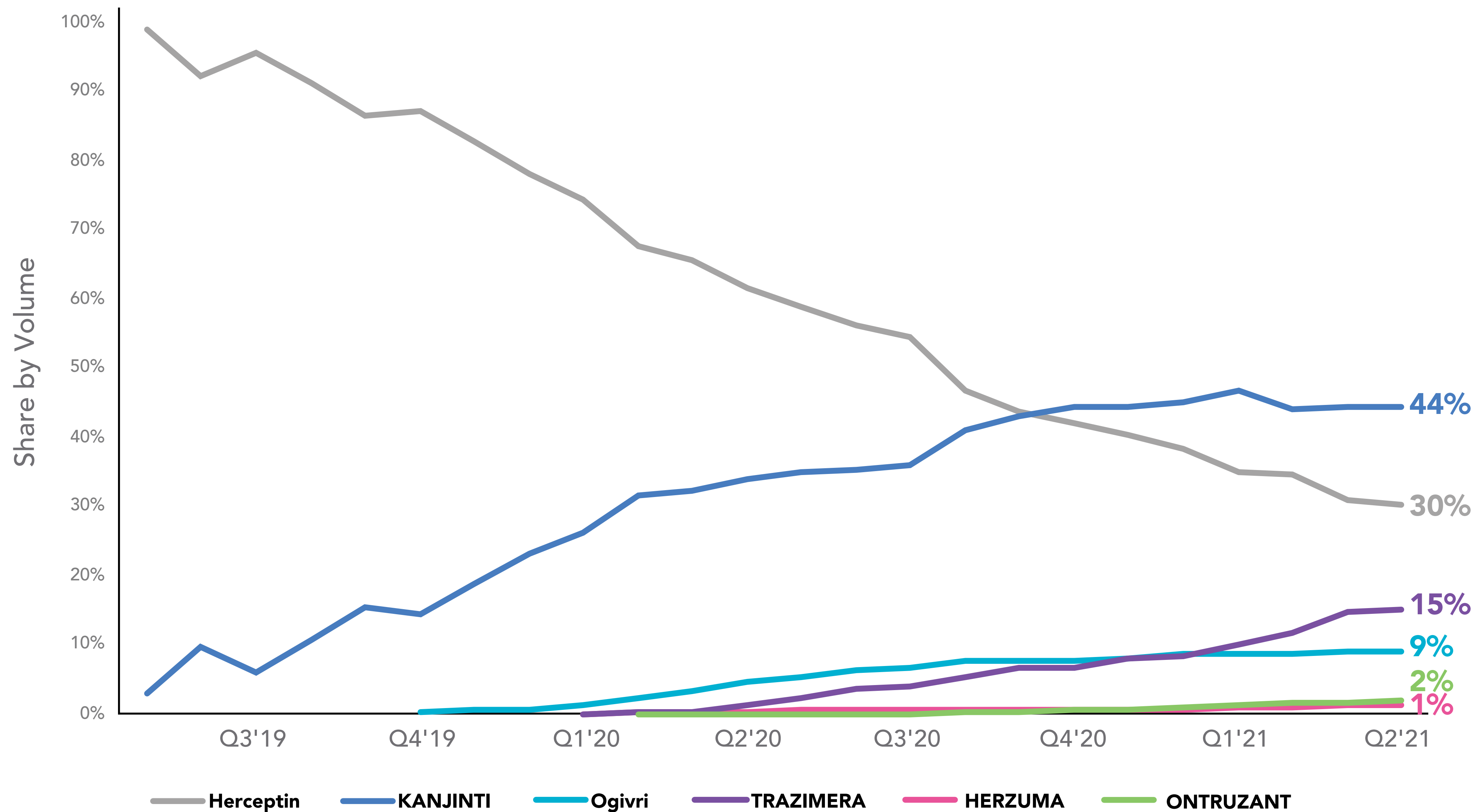


## Trastuzumab

As seen in **Figure 13**, there has been a strong adoption of trastuzumab biosimilars. Within 18 months after launching, KANJINTI captured more share than the reference product Herceptin.

**Two years after the first launch, biosimilars now account for 70% share of all trastuzumab products.**

**Figure 13.** Biosimilar Uptake Curve for Trastuzumab Products<sup>5</sup>



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See [Full Prescribing Information](#) for complete risk information.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY THERAPEUTICS



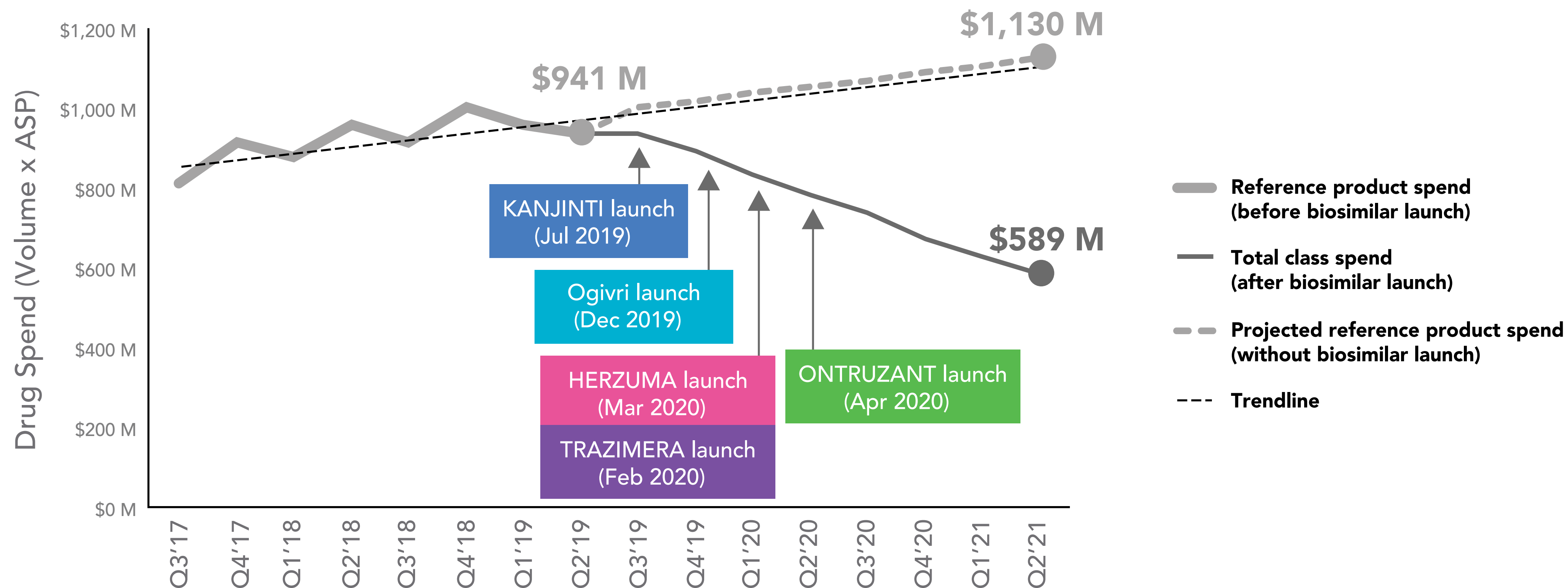
## Trastuzumab

**Figure 14** shows the total drug spend for trastuzumab with biosimilar launches, compared to the projected drug spend in the absence of biosimilar competition.

**The cumulative savings in drug spend for trastuzumab from the Herceptin biosimilar launch in Q3 2019 to Q2 2021 is estimated to be \$2.5 billion.**

**Without biosimilar competition, projected 2021 spending on trastuzumab could have been nearly double current levels.**

**Figure 14.** Comparison of Trastuzumab Drug Spend With vs Without Biosimilar Competition<sup>3</sup>



Please [click here](#) for Boxed Warning information for KANJINTI.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price.  
The quarterly drug spend for each product is estimated as: Drug spend=ASPxNormalized unit volume. The estimated spend for the reference product (after biosimilar launch) is trended out based on historical spend for the reference product before biosimilar launch.  
Sources: AnalySource, Integrated Weekly Sales Data (IQVIA DDD + Chargeback).

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

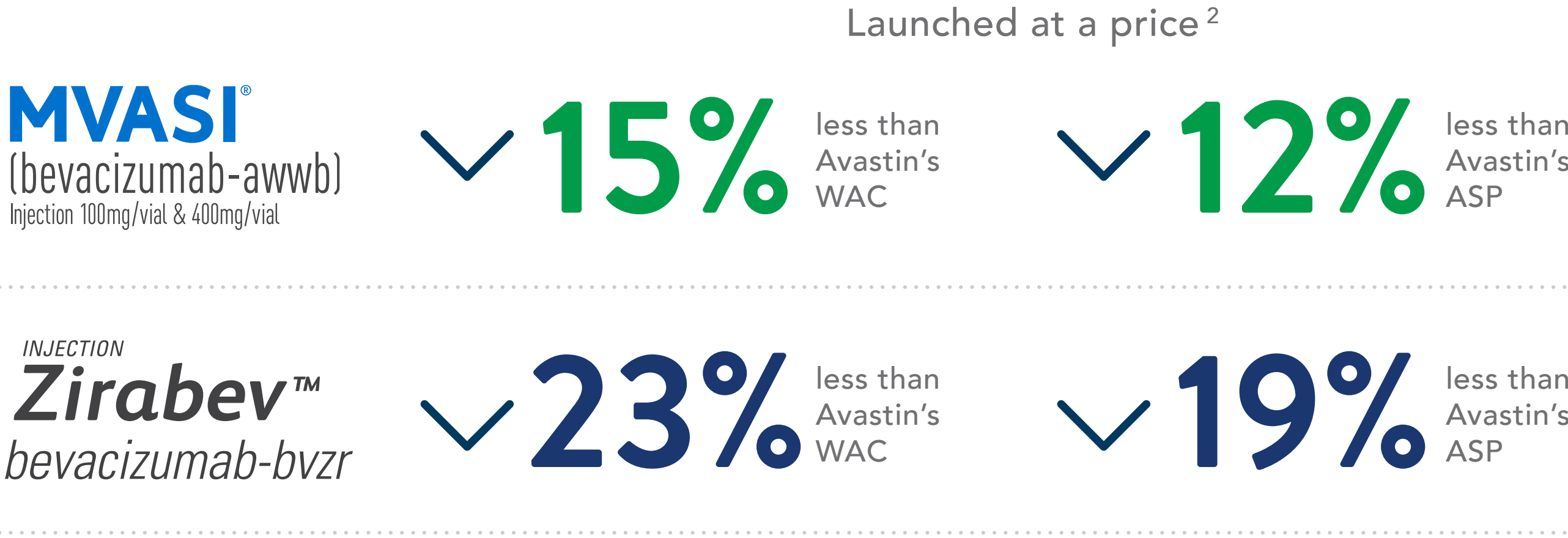
REFERENCES



# ONCOLOGY THERAPEUTICS

## Bevacizumab

Since 2019, 2 biosimilars have launched to the reference product Avastin (bevacizumab):



● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

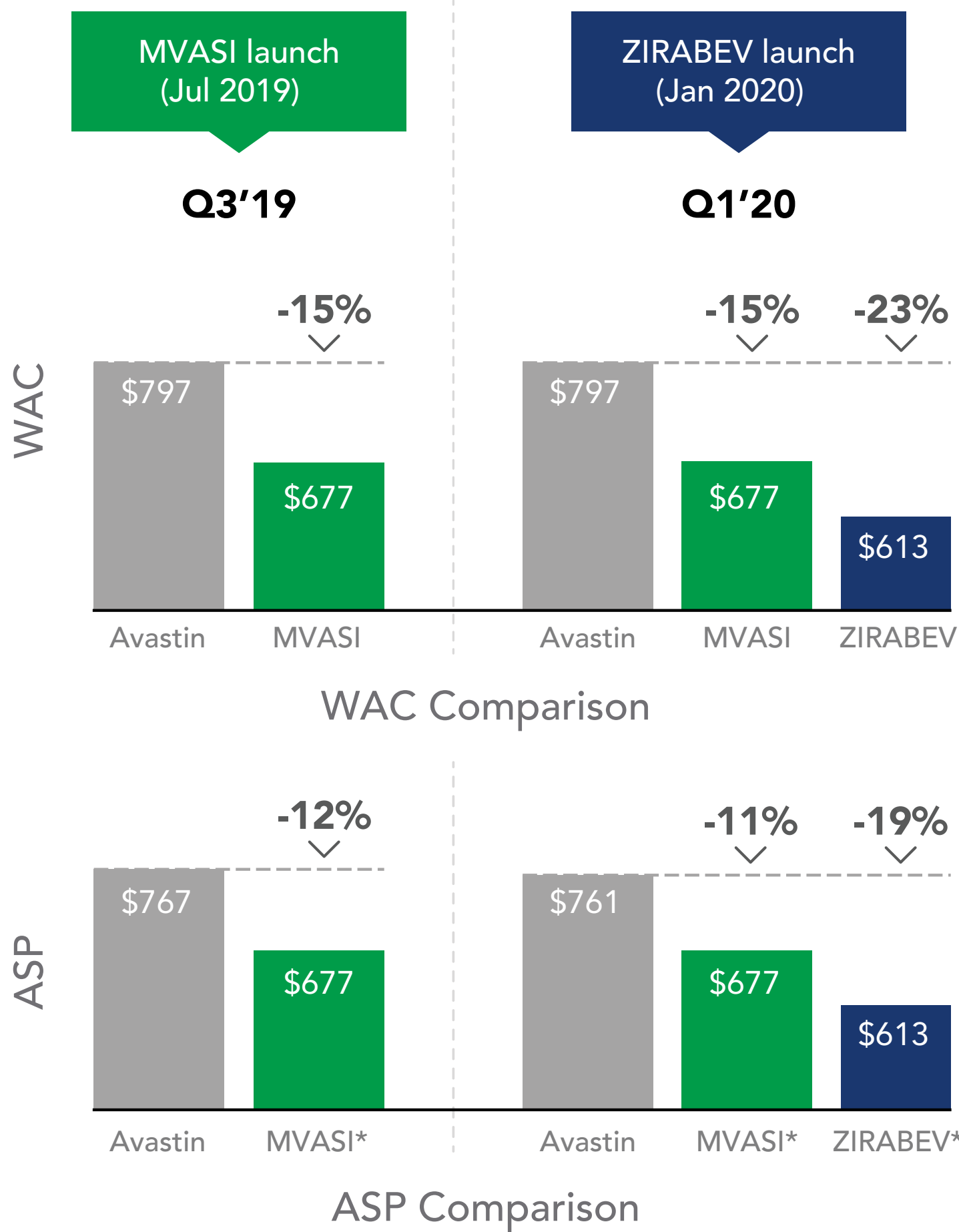
Key: ASP – average sales price; WAC – wholesale acquisition cost.

# ONCOLOGY THERAPEUTICS

## Bevacizumab

As **Figure 15** shows, in addition to both biosimilars launching at WAC and ASP discounts to the reference product, ZIRABEV—the second biosimilar to Avastin—launched at a discount to the first biosimilar, MVASI.

**Figure 15.** WAC and ASP of Bevacizumab Biosimilars Relative to Reference Product at Launch<sup>2</sup>



Key: ASP – average sales price; WAC – wholesale acquisition cost.  
 \*ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
 Source: AnalySource.



INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY THERAPEUTICS

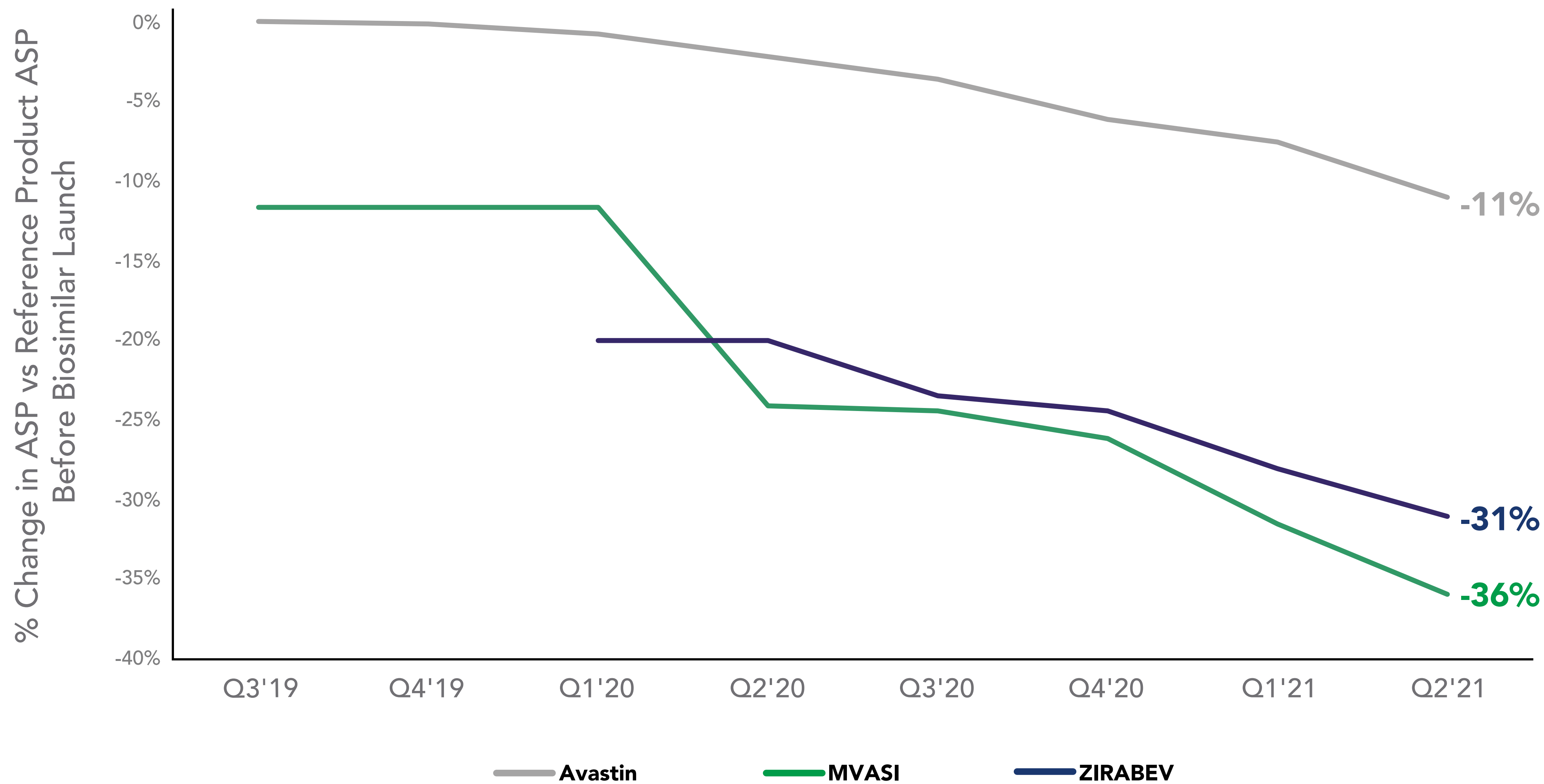


## Bevacizumab

**Figure 16** shows the percentage change in the price of biosimilars over time when compared to the reference product's ASP at the time that the first biosimilar to Avastin was launched.

**Two years after the first launch, the price of bevacizumab biosimilars is now 22% to 29% lower than the price of reference product Avastin in Q2 2021.**

**Figure 16.** ASP of Bevacizumab Products at Biosimilars' Launches<sup>2</sup>



Key: ASP – average sales price; WAC – wholesale acquisition cost.  
Biosimilar WAC is used for comparing against reference product ASP until biosimilar ASP is available.  
Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY THERAPEUTICS

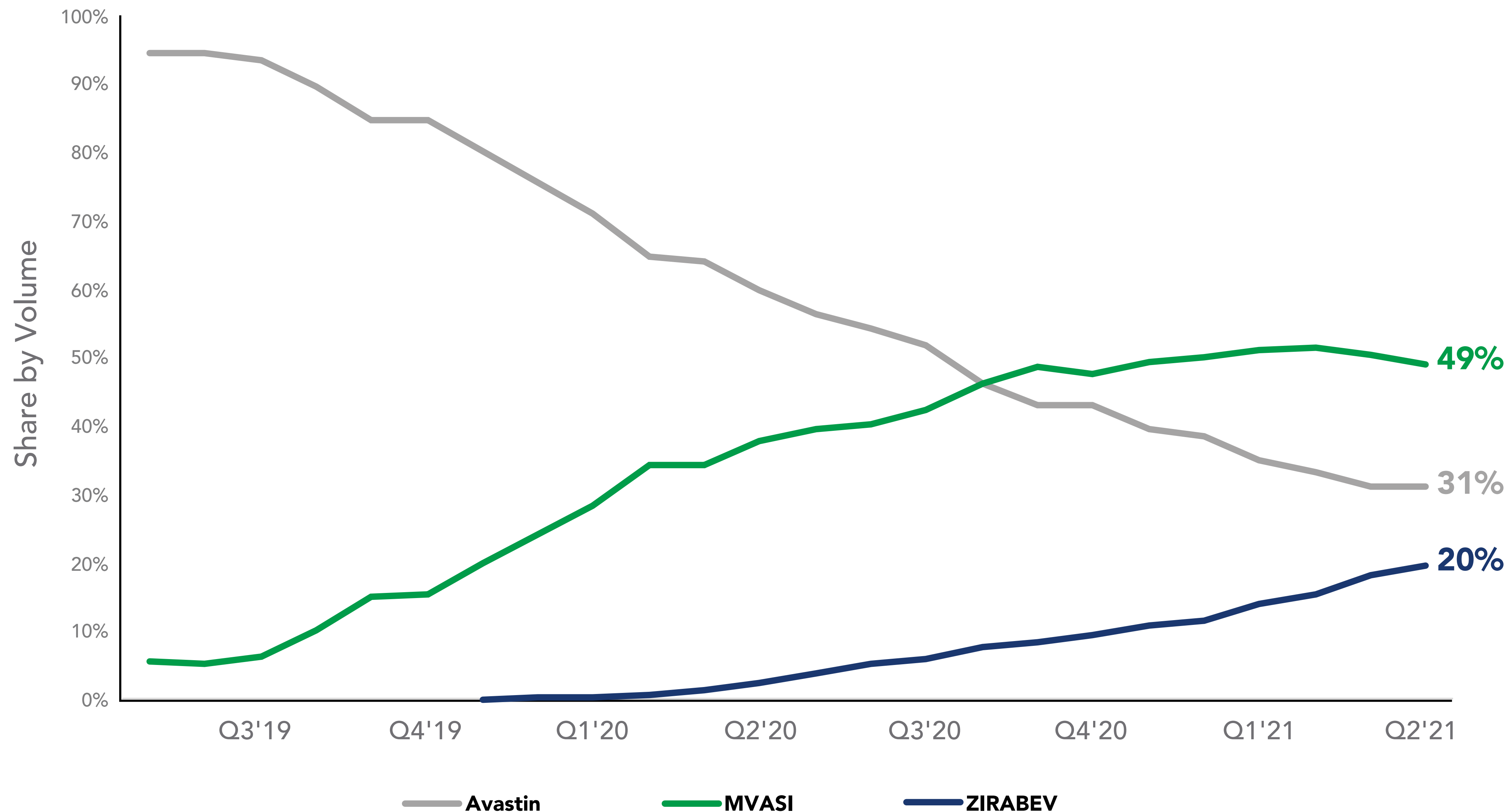


## Bevacizumab

As seen in **Figure 17**, there has been a strong adoption of bevacizumab biosimilars. Within 16 months after launching, MVASI captured more share than the reference product Avastin.

**Two years after the first launch, biosimilars now account for 69% share of all bevacizumab products.**

**Figure 17.** Biosimilar Uptake Curve for Bevacizumab Products<sup>5</sup>



INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY THERAPEUTICS

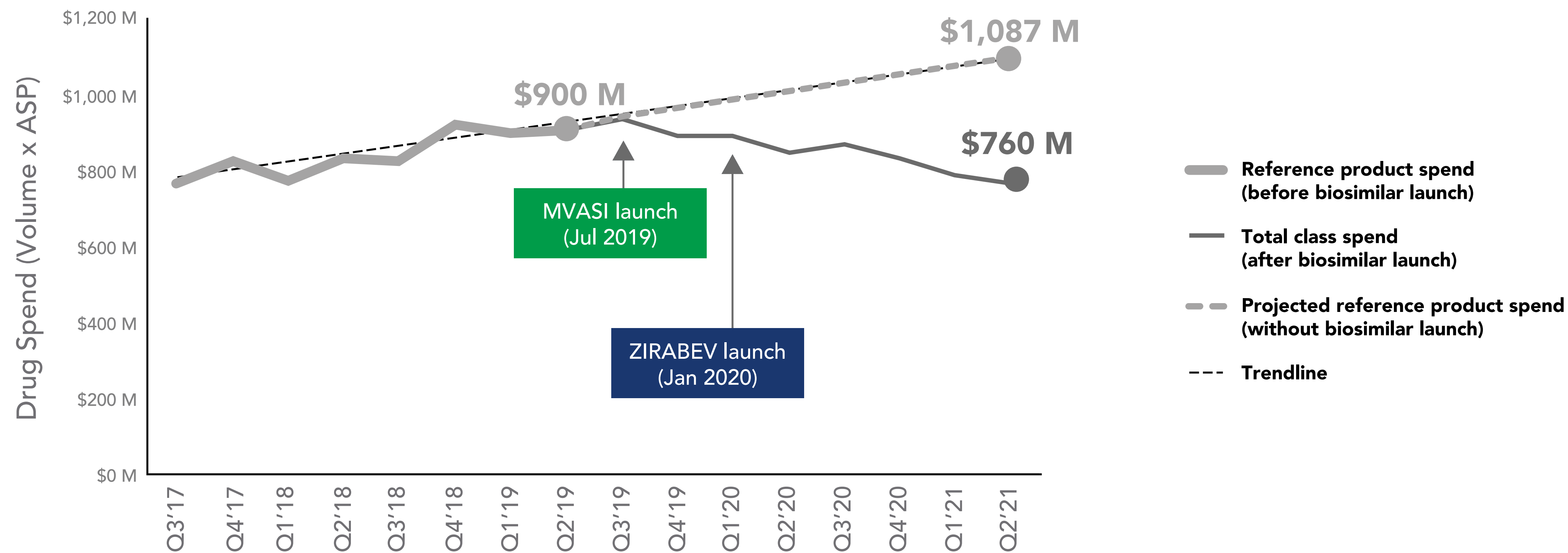


## Bevacizumab

**Figure 18** shows the total drug spend for bevacizumab with biosimilar launches, compared to the projected drug spend in the absence of biosimilar competition.

**The cumulative savings in drug spend for bevacizumab from the first Avastin biosimilar launch in Q3 2019 to Q2 2021 is estimated to be \$1.3 billion.**

**Figure 18.** Comparison of Bevacizumab Drug Spend With vs Without Biosimilar Competition<sup>3</sup>



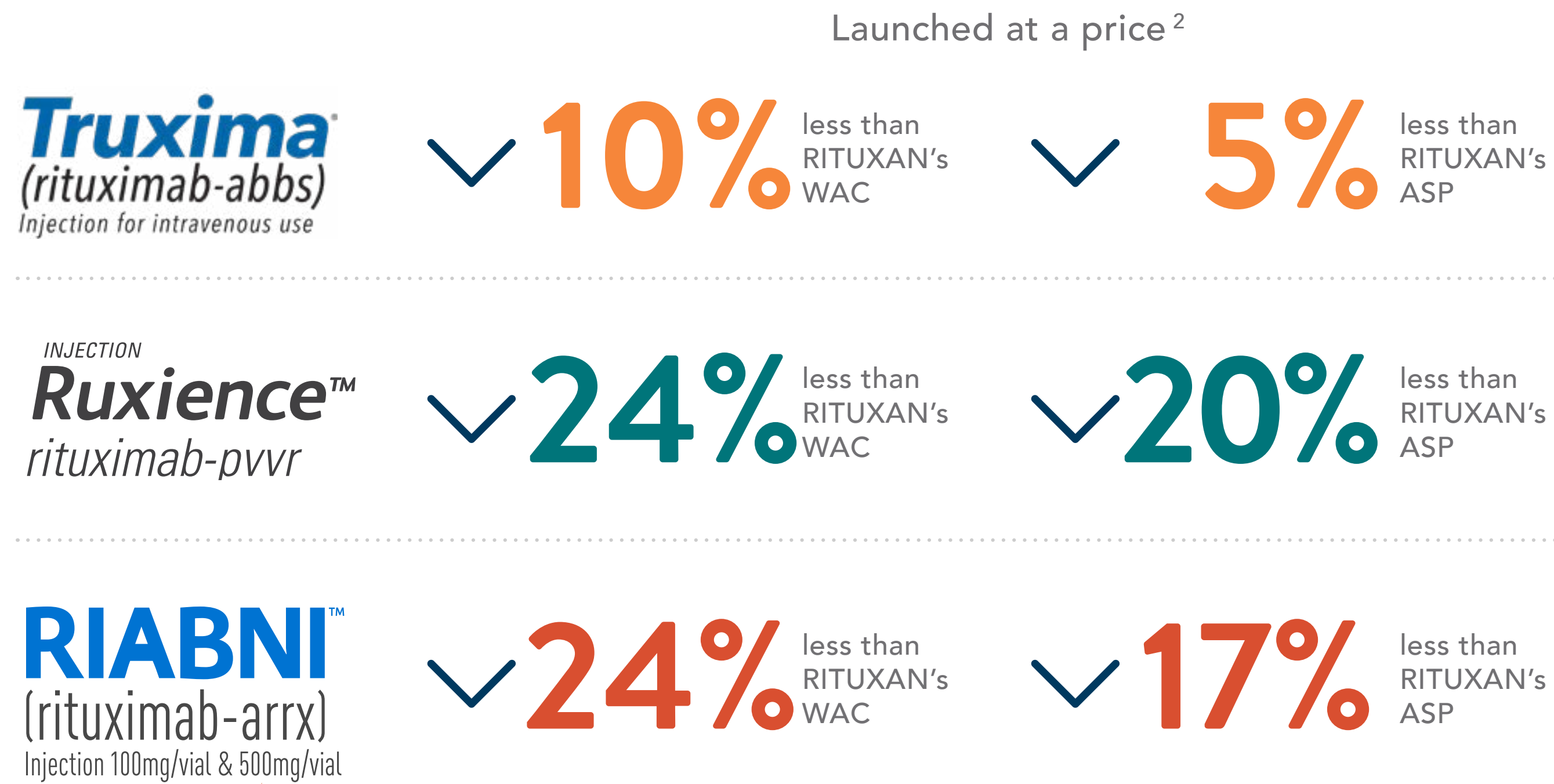
- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

Key: ASP – average sales price.  
 The quarterly drug spend for each product is estimated as: Drug spend=ASPxNormalized unit volume. The estimated spend for the reference product (after biosimilar launch) is trended out based on historical spend for the reference product before biosimilar launch.  
 Sources: AnalySource, Integrated Weekly Sales Data (IQVIA DDD + Chargeback).

# ONCOLOGY THERAPEUTICS

## Rituximab

Three biosimilars have launched—in 2019, 2020, and 2021—to the reference product RITUXAN (rituximab):



Please [click here](#) for Boxed Warning information for RIABNI.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.



- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

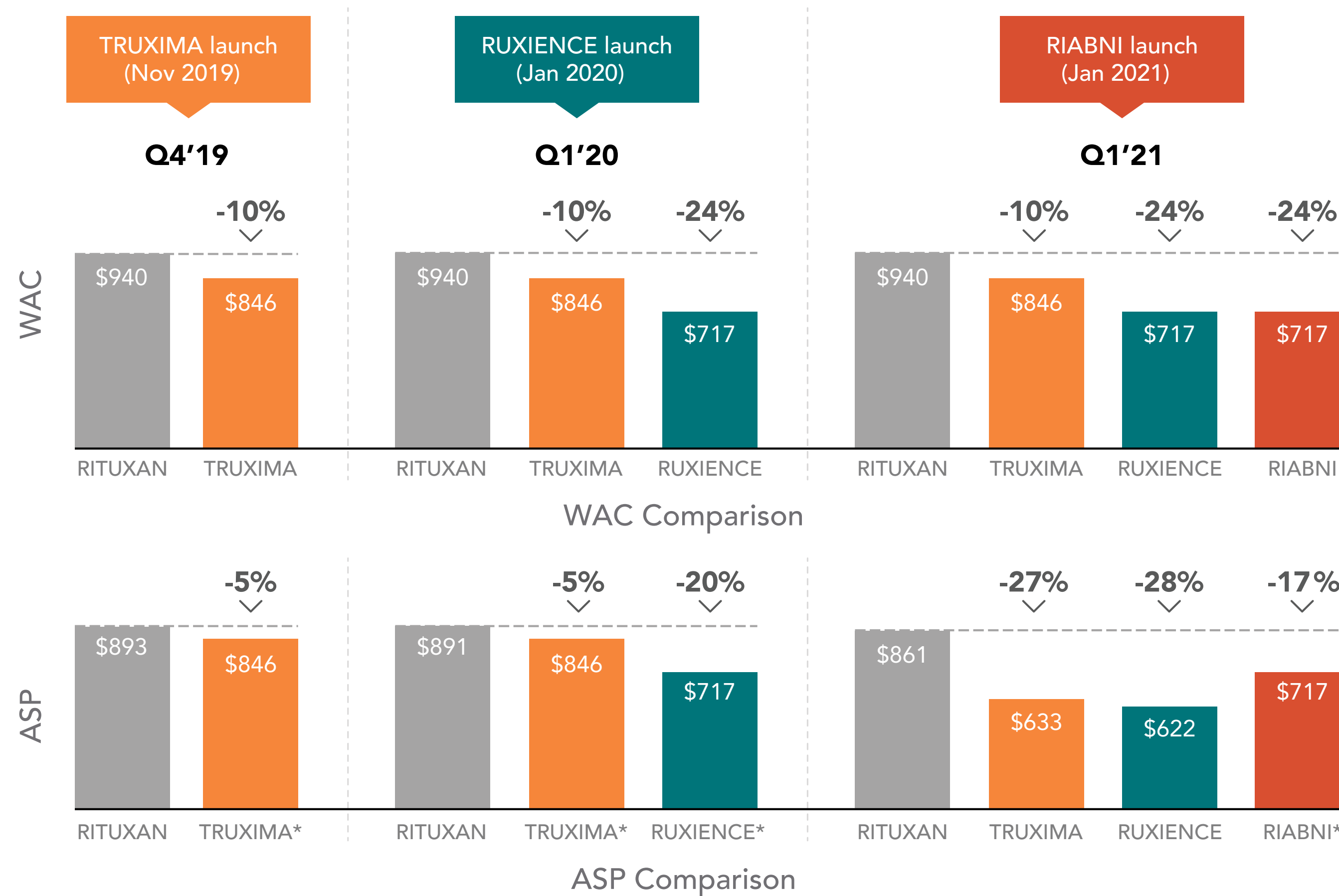
# ONCOLOGY THERAPEUTICS



## Rituximab

As **Figure 19** shows, in addition to all biosimilars launching at WAC and ASP discounts to the reference product, subsequent biosimilars launching after 2019 did so at a discount to the first rituximab biosimilar, TRUXIMA.

**Figure 19.** WAC and ASP of Rituximab Biosimilars Relative to Reference Product at Launch<sup>2</sup>



Please [click here](#) for Boxed Warning information for RIABNI.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
\*ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY THERAPEUTICS

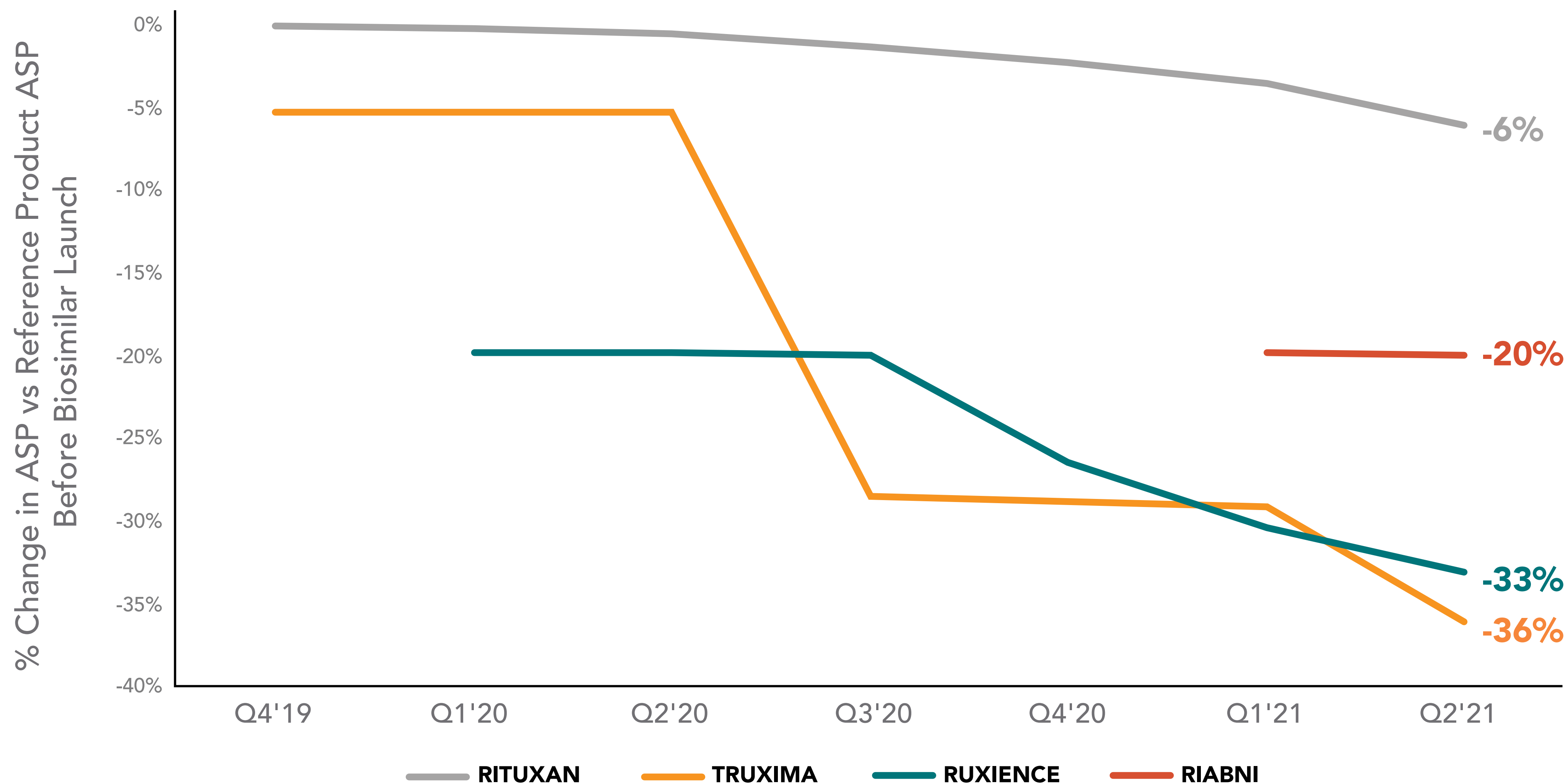


## Rituximab

**Figure 20** shows the percentage change in the price of biosimilars over time when compared to the reference product's ASP at the time that the first rituximab biosimilar launched.

**In under 2 years after the first launch, the price of rituximab biosimilars is now 15% to 32% lower than the price of reference product RITUXAN in Q2 2021.**

**Figure 20.** ASP of Rituximab Products at Biosimilars' Launches<sup>2</sup>



Please [click here](#) for Boxed Warning information for RIABNI.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
Biosimilar WAC is used for comparing against reference product ASP until biosimilar ASP is available.  
Source: AnalySource.

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES



# ONCOLOGY THERAPEUTICS

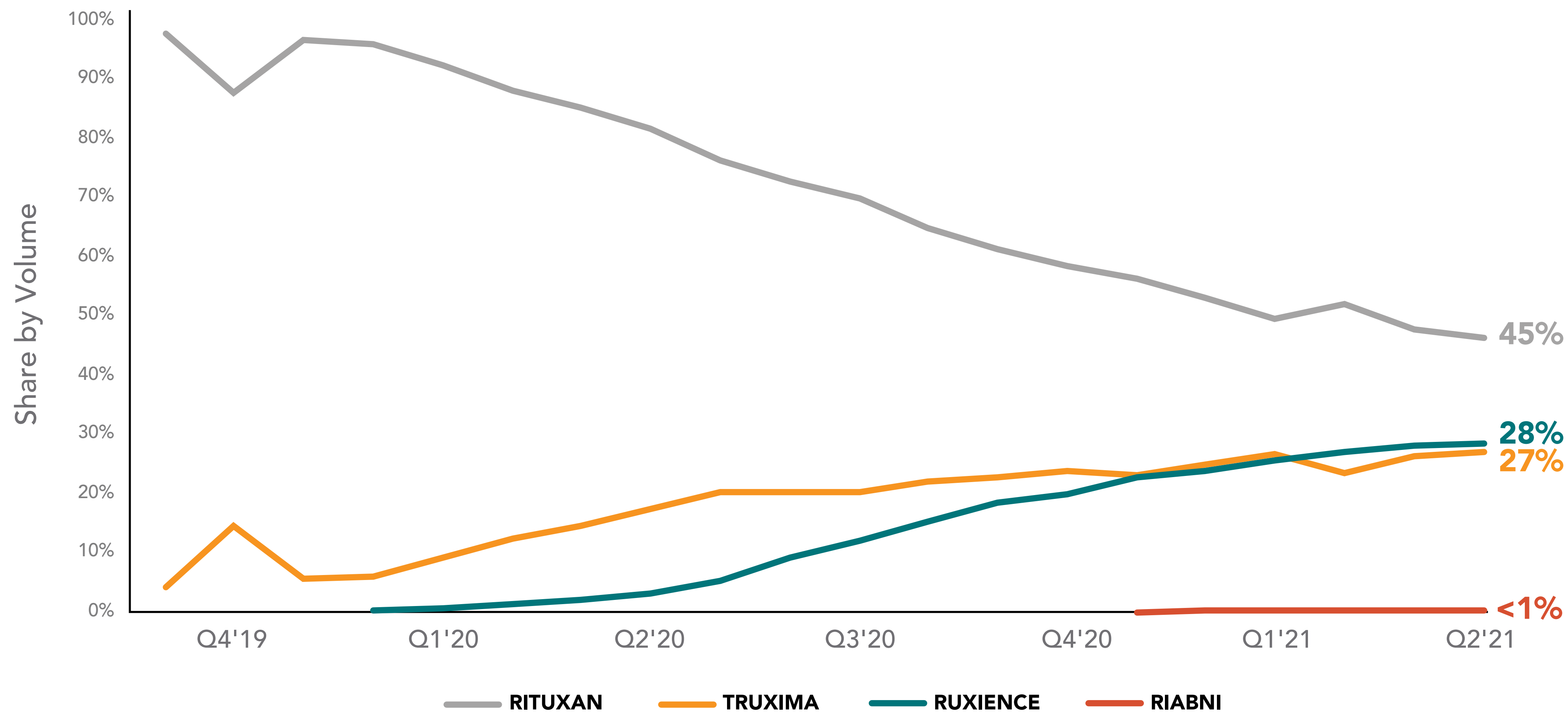


## Rituximab

As seen in **Figure 21**, there has been a strong adoption of rituximab biosimilars, particularly after the second and third biosimilars launched beginning in 2020.

**In under 2 years after the first launch, biosimilars now account for 55% share of all rituximab products.**

**Figure 21.** Biosimilar Uptake Curve for Rituximab Products<sup>5</sup>



Please [click here](#) for Boxed Warning information for RIABNI.  
See [Full Prescribing Information](#) for complete risk information.

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# ONCOLOGY THERAPEUTICS

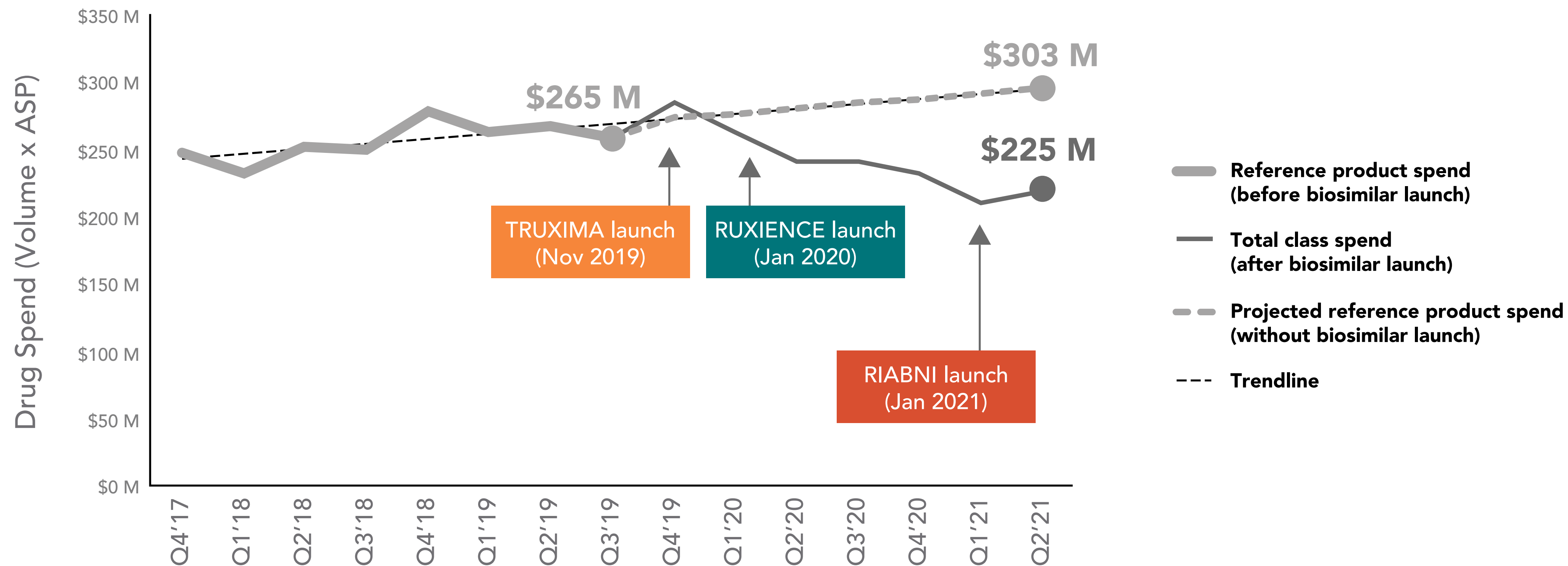


## Rituximab

**Figure 22** shows the total drug spend for rituximab with biosimilar launches, compared to the projected drug spend in the absence of biosimilar competition. The total spend for rituximab started to decline following the launch of the first RITUXAN biosimilar TRUXIMA in Q4 2019, and continued to decline after the second biosimilar launch in Q1 2020.

**Spending on rituximab has decreased following the launch of RITUXAN biosimilars in Q4 2019, contributing to \$304 million in cumulative savings.**

**Figure 22.** Comparison of Rituximab Drug Spend With vs Without Biosimilar Competition<sup>3</sup>



Please [click here](#) for Boxed Warning information for RIABNI.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price.  
The quarterly drug spend for each product is estimated as: Drug spend=ASPxNormalized unit volume. The estimated spend for the reference product (after biosimilar launch) is trended out based on historical spend for the reference product before biosimilar launch  
Sources: AnalySource, Integrated Weekly Sales Data (IQVIA DDD + Chargeback).

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# ONCOLOGY SUPPORTIVE CARE



The biosimilars available for oncology supportive care consist of **pegfilgrastim** and **filgrastim** products. For each, we discuss:

- 1** WAC and ASP of the biosimilar at launch compared to the reference product
- 2** ASP for the reference product and biosimilars since launch
- 3** Biosimilar uptake
- 4** Estimated difference in total drug spend after biosimilar competition\*

*Oncology supportive care is the most mature US biosimilar category.*

The FDA approved GRANIX in 2012, though not as a biosimilar under the pathway created by the BPCIA.<sup>32</sup> ZARXIO was the first biosimilar approved in the US (in 2015), and also the first biosimilar to become commercially available (also in 2015).<sup>33</sup> As such, this category provides insights into how biosimilars and their reference products change over time, as well as how biosimilars may gain share over a period of 5 years.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

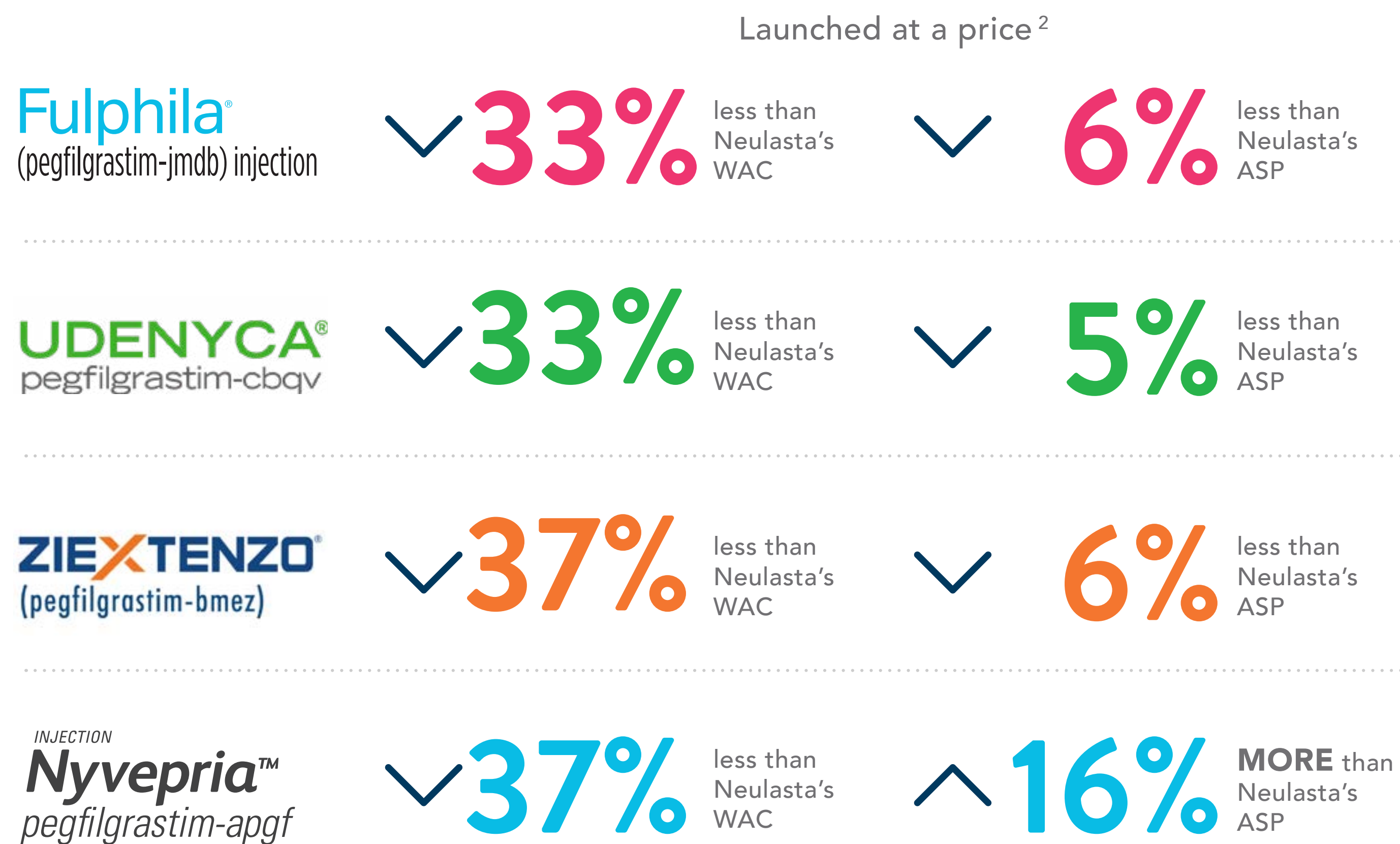
● REFERENCES



# ONCOLOGY SUPPORTIVE CARE

## Pegfilgrastim

Four biosimilars have launched since 2018 to the reference product Neulasta (pegfilgrastim):



See Neulasta [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



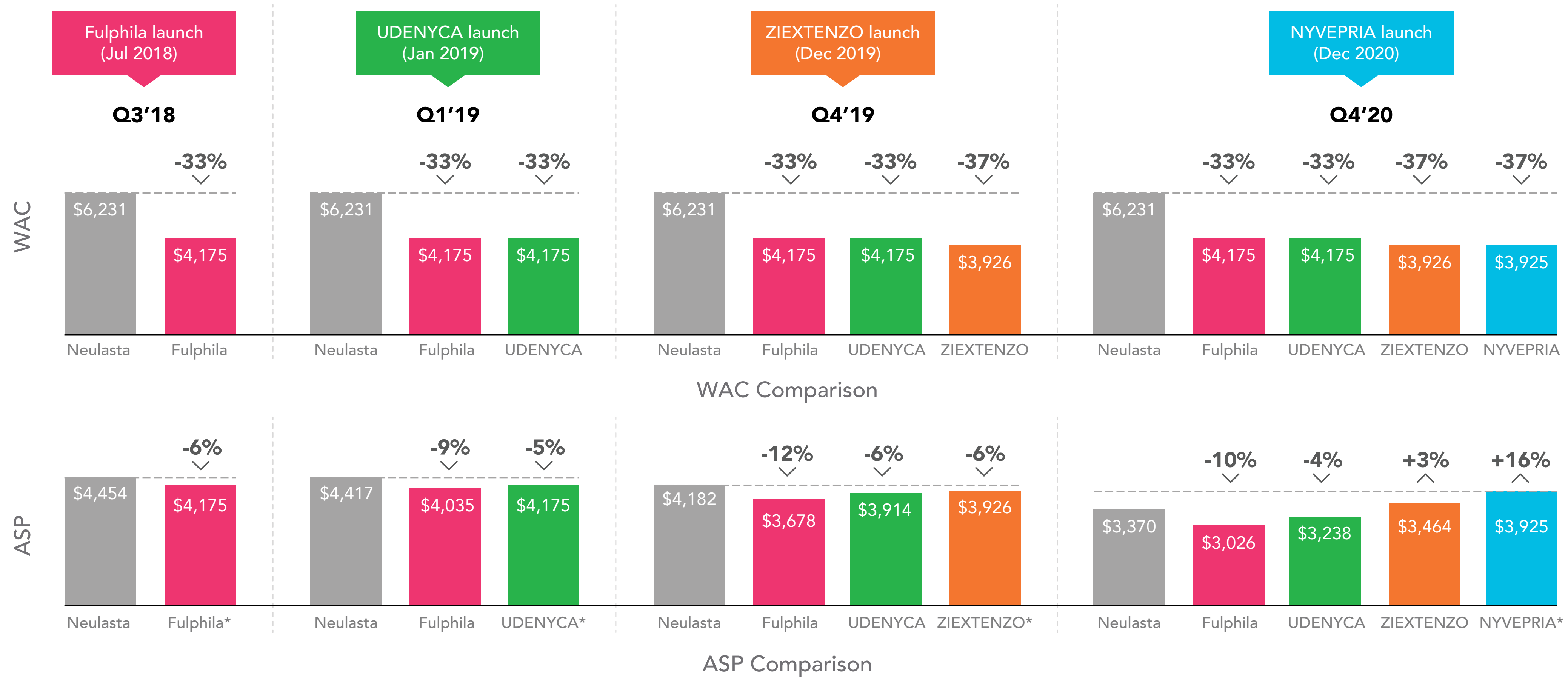
# ONCOLOGY SUPPORTIVE CARE



## Pegfilgrastim

As **Figure 23** shows, all 4 biosimilars launched between a 33% to 37% discount to the reference product Neulasta's WAC. While the first 3 pegfilgrastim biosimilars launched at discounts, the fourth pegfilgrastim biosimilar launched at a premium to the ASP of the reference product. The second, third, and fourth pegfilgrastim biosimilars also launched at premiums to the ASP of Fulphila (the first pegfilgrastim biosimilar).

**Figure 23.** WAC and ASP of Pegfilgrastim Biosimilars Relative to Reference Product at Launch<sup>2</sup>



See Neulasta [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
 \*ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
 Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY SUPPORTIVE CARE

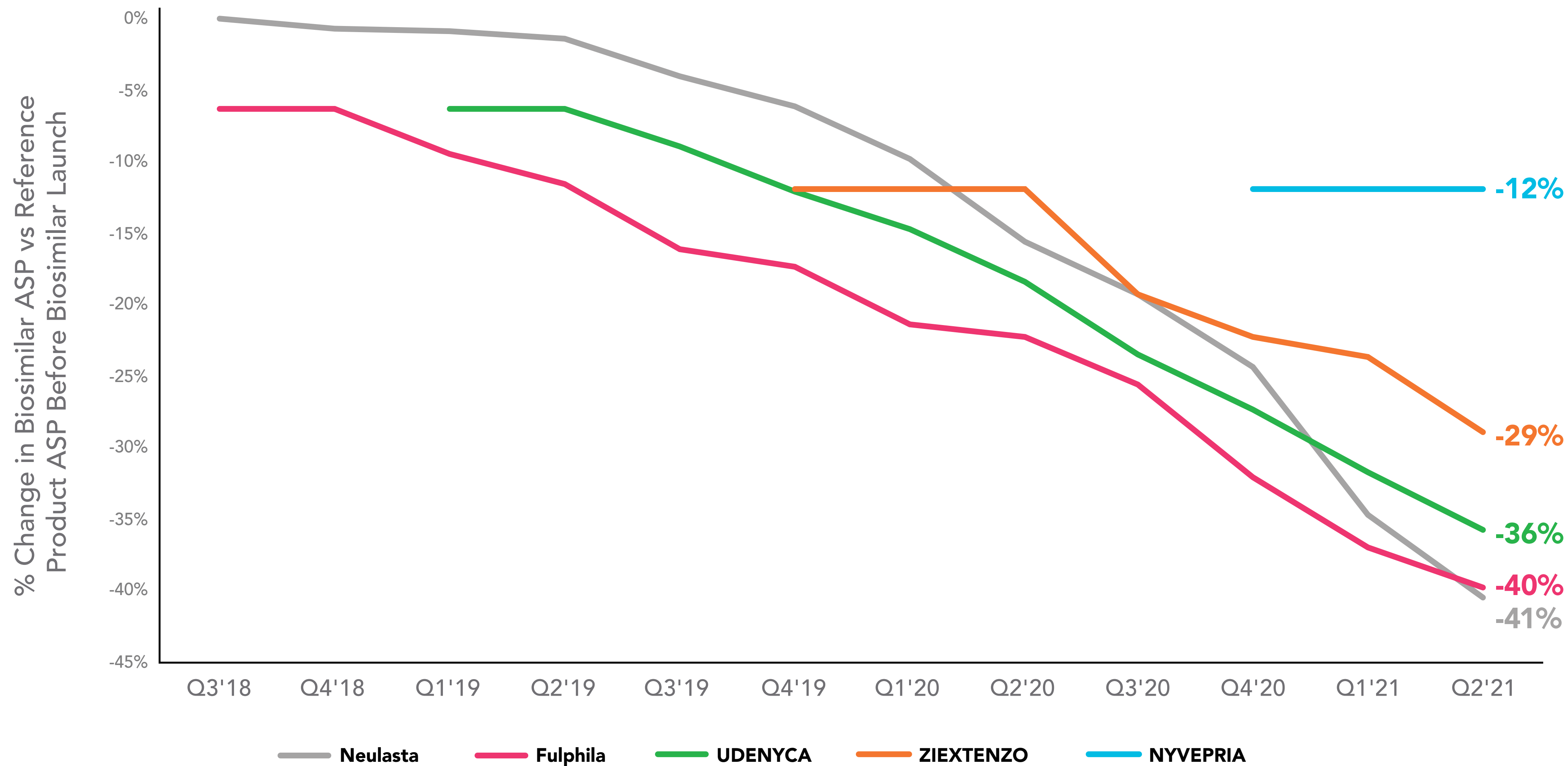


## Pegfilgrastim

**Figure 24** shows the percentage change in the price of biosimilars over time when compared to the reference product's ASP at the time that the first pegfilgrastim biosimilar launched.

**ASPs for all pegfilgrastim products have continued to decline over time, particularly in the last 18 months with 2 additional biosimilar launches. The reference product Neulasta's price has declined by 40% over the last 3 years since the first pegfilgrastim biosimilar was launched.**

**Figure 24.** ASP of Pegfilgrastim Products at Biosimilars' Launches<sup>2</sup>



See Neulasta [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
 Biosimilar WAC is used for comparing against reference product ASP until biosimilar ASP is available.  
 Source: AnalySource.

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# ONCOLOGY SUPPORTIVE CARE

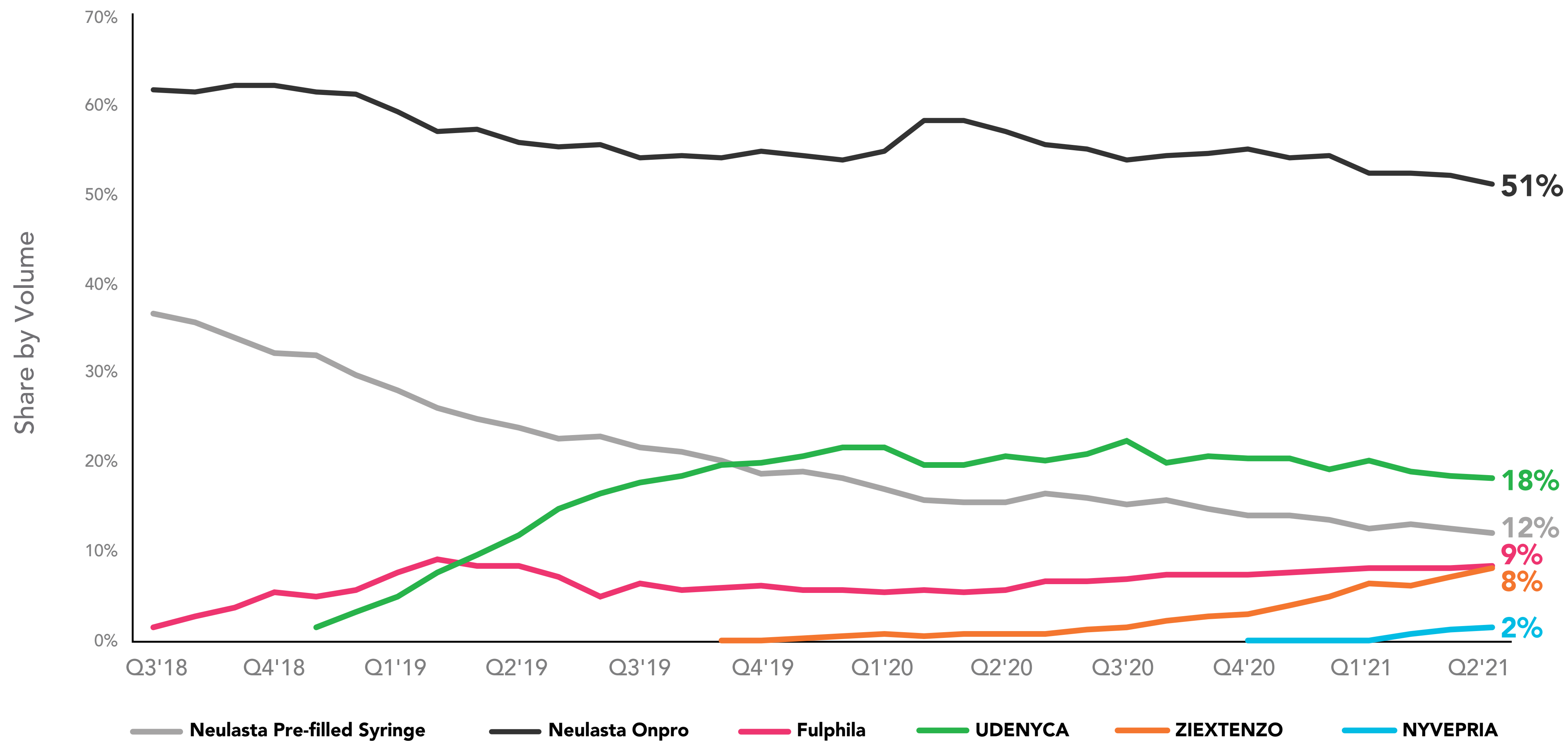


## Pegfilgrastim

As seen in **Figure 25**, pegfilgrastim biosimilars show a different uptake pattern than other biosimilars, where the first biosimilar to launch captured the most share. By comparison, the leading pegfilgrastim biosimilar by share is UDENYCA, which was the second pegfilgrastim biosimilar to launch.

**With 4 biosimilars now launched and available in the US, biosimilars account for 37% share of all pegfilgrastim products.**

**Figure 25.** Biosimilar Uptake Curve for Pegfilgrastim Products<sup>5</sup>



See Neulasta [Full Prescribing Information](#) for complete risk information.

Key: US – United States.  
Source: OBU Customer Data Pack Weekly (IQVIA DDD + Chargeback).

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# ONCOLOGY SUPPORTIVE CARE

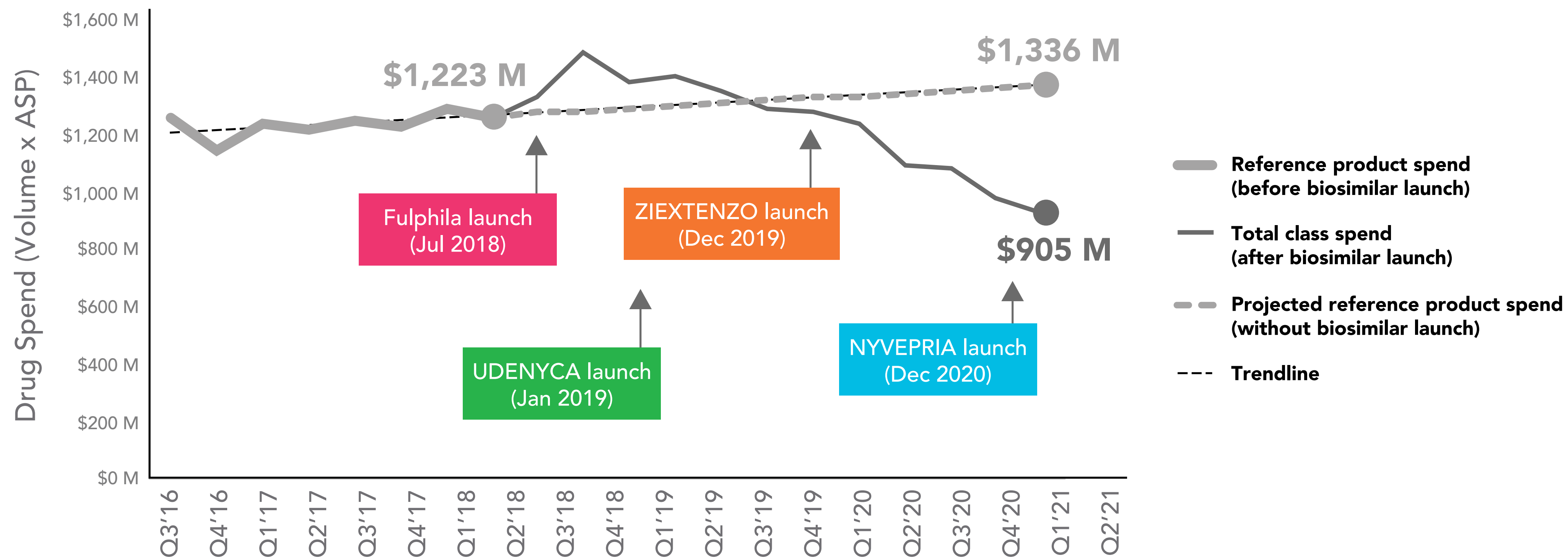


## Pegfilgrastim

**Figure 26** shows the total drug spend for pegfilgrastim with biosimilar launches, compared to the projected drug spend in the absence of biosimilar competition.

**After an initial increase, drug spend for pegfilgrastim has steadily declined overall since Q4 2018, resulting in a cumulative reduction of \$990 million.**

**Figure 26.** Comparison of Pegfilgrastim Drug Spend With vs Without Biosimilar Competition<sup>3</sup>



See Neulasta [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price.  
 The quarterly drug spend for each product is estimated as: Drug spend=ASPxNormalized unit volume. The estimated spend for the reference product (after biosimilar launch) is trended out based on historical spend for the reference product before biosimilar launch.  
 Sources: AnalySource, Integrated Weekly Sales Data (IQVIA DDD + Chargeback).

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

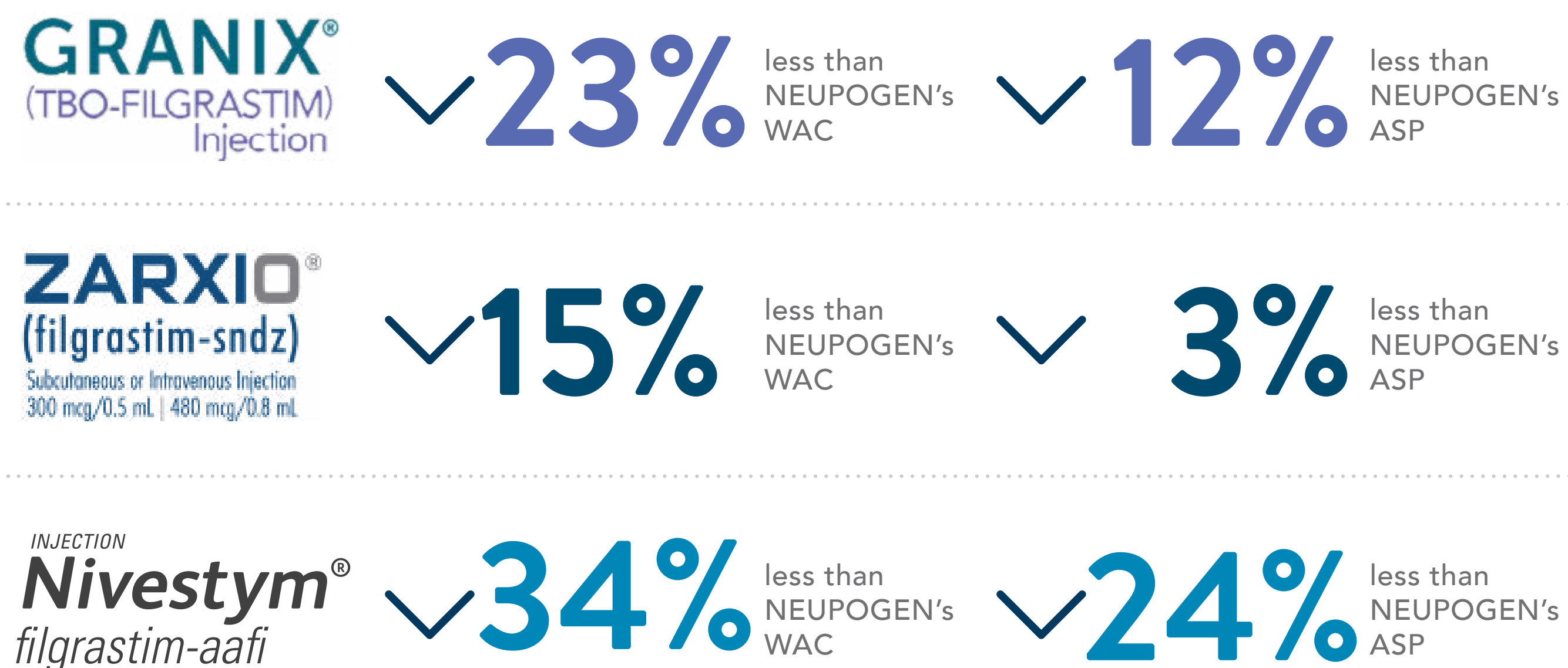


# ONCOLOGY SUPPORTIVE CARE

## Filgrastim

Two biosimilars have been approved and launched since 2015 along with GRANIX in 2013 to the reference product NEUPOGEN (filgrastim):

Launched at a price<sup>2</sup>



**GRANIX is not a biosimilar. It was approved under a stand-alone Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.<sup>32</sup>**

See NEUPOGEN [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; FDA – Food and Drug Administration; WAC – wholesale acquisition cost.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



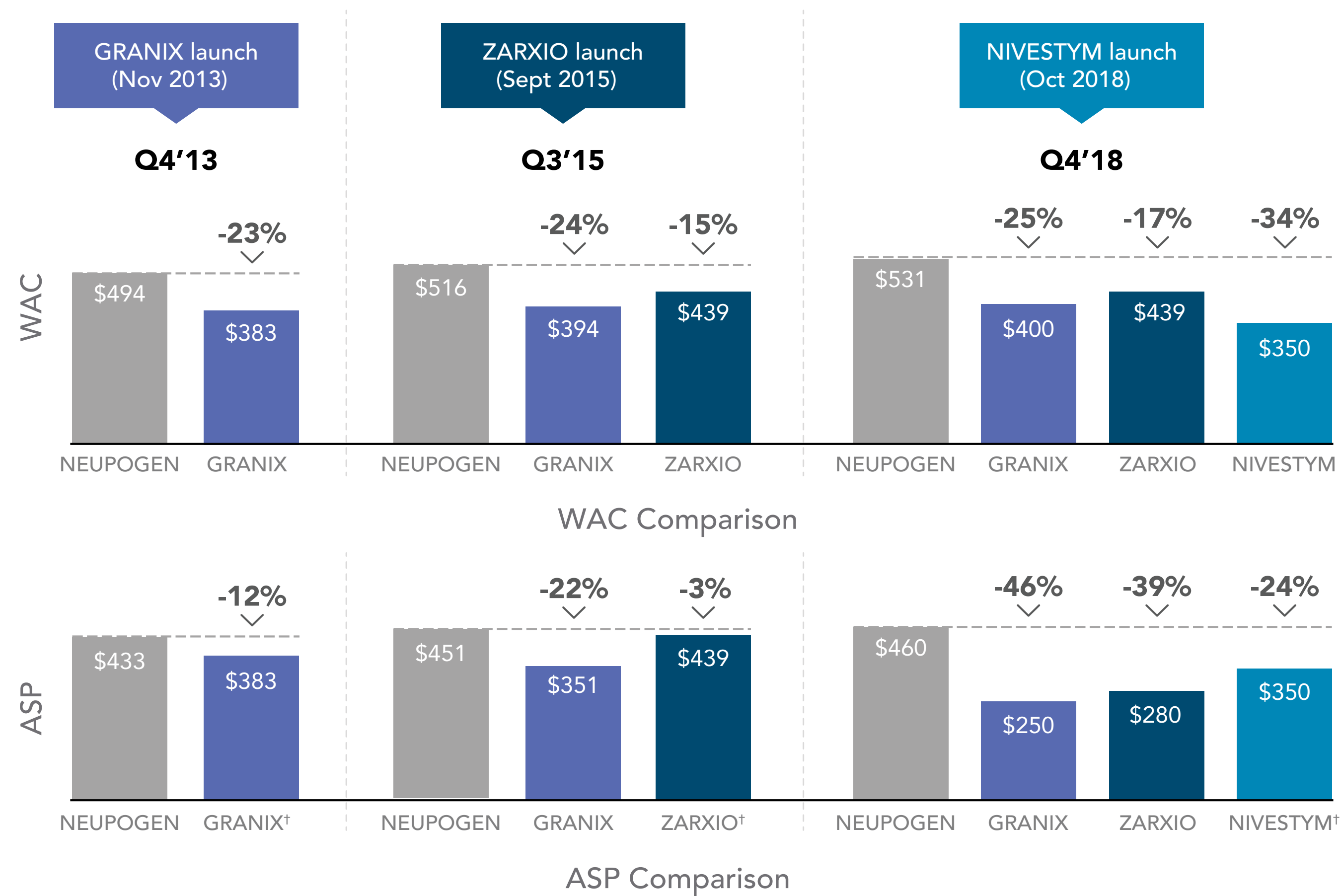
# ONCOLOGY SUPPORTIVE CARE



## Filgrastim

As **Figure 27** shows, in addition to both biosimilars and GRANIX\* launching at WAC and ASP discounts to the reference product, NIVESTYM launched at a discounted WAC to its predecessor ZARXIO.

**Figure 27.** WAC and ASP of GRANIX and Filgrastim Biosimilars Relative to Reference Product at Launch<sup>2</sup>



See **NEUPOGEN Full Prescribing Information** for complete risk information.

Key: ASP – average sales price; FDA – Food and Drug Administration; WAC – wholesale acquisition cost.  
 \*GRANIX is not a biosimilar. It was approved under a full Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.  
 †ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
 Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# ONCOLOGY SUPPORTIVE CARE

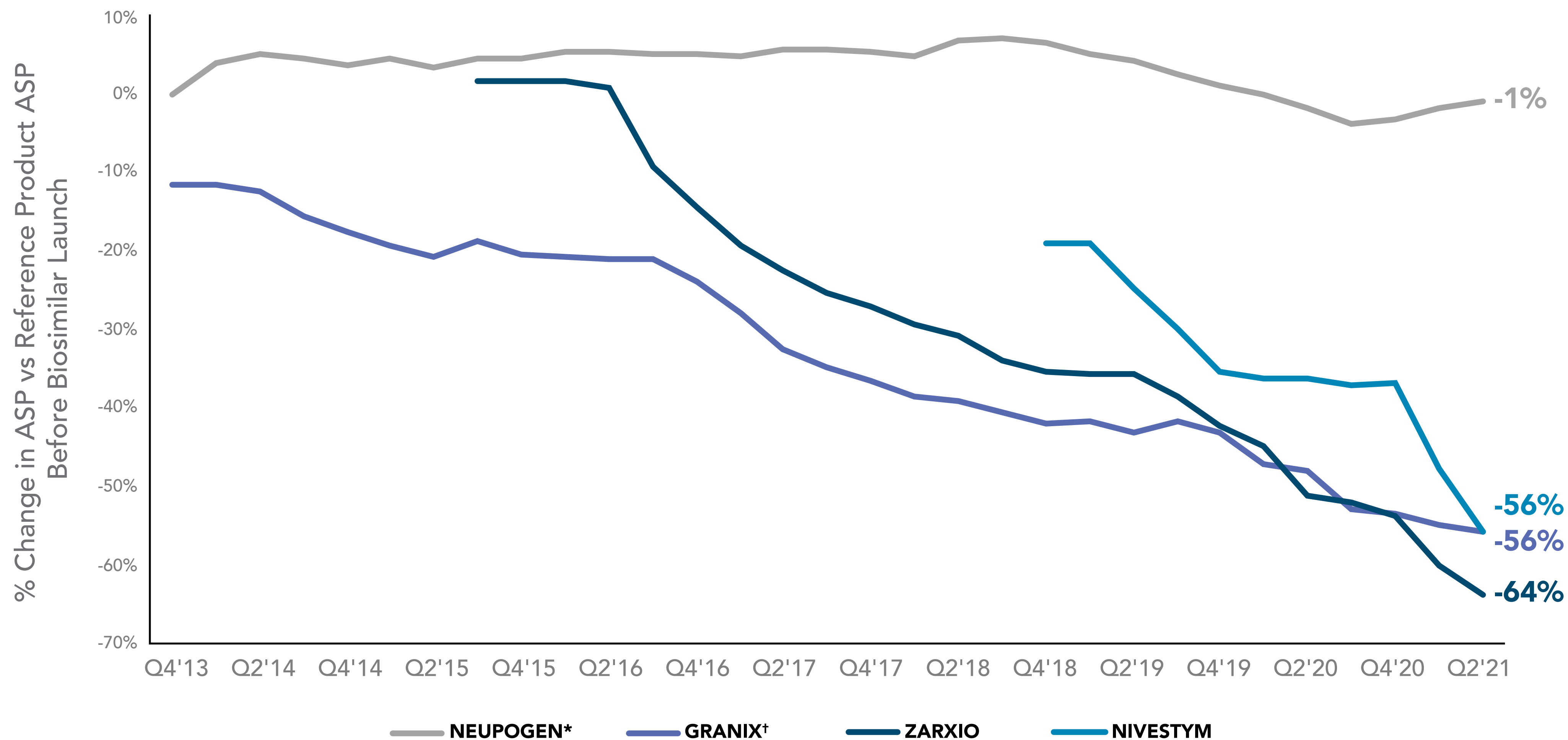


## Filgrastim

**Figure 28** shows the percentage change in price over time when compared to NEUPOGEN's ASP at the time GRANIX launched. By 2021, both filgrastim biosimilars and GRANIX saw significant decreases in their ASPs, while the ASP for reference product NEUPOGEN has remained relatively stable.

**The price of filgrastim biosimilars is now 56% to 64% lower than the price of reference product NEUPOGEN in Q2 2021.**

**Figure 28.** ASP of Filgrastim Products at Biosimilars' Launches<sup>2</sup>



See [NEUPOGEN Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; FDA – Food and Drug Administration; WAC – wholesale acquisition cost.

\*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.

†GRANIX is not a biosimilar. It was approved under a full Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.

Biosimilar WAC is used for comparing against reference product ASP until biosimilar ASP is available.

Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES



# ONCOLOGY SUPPORTIVE CARE

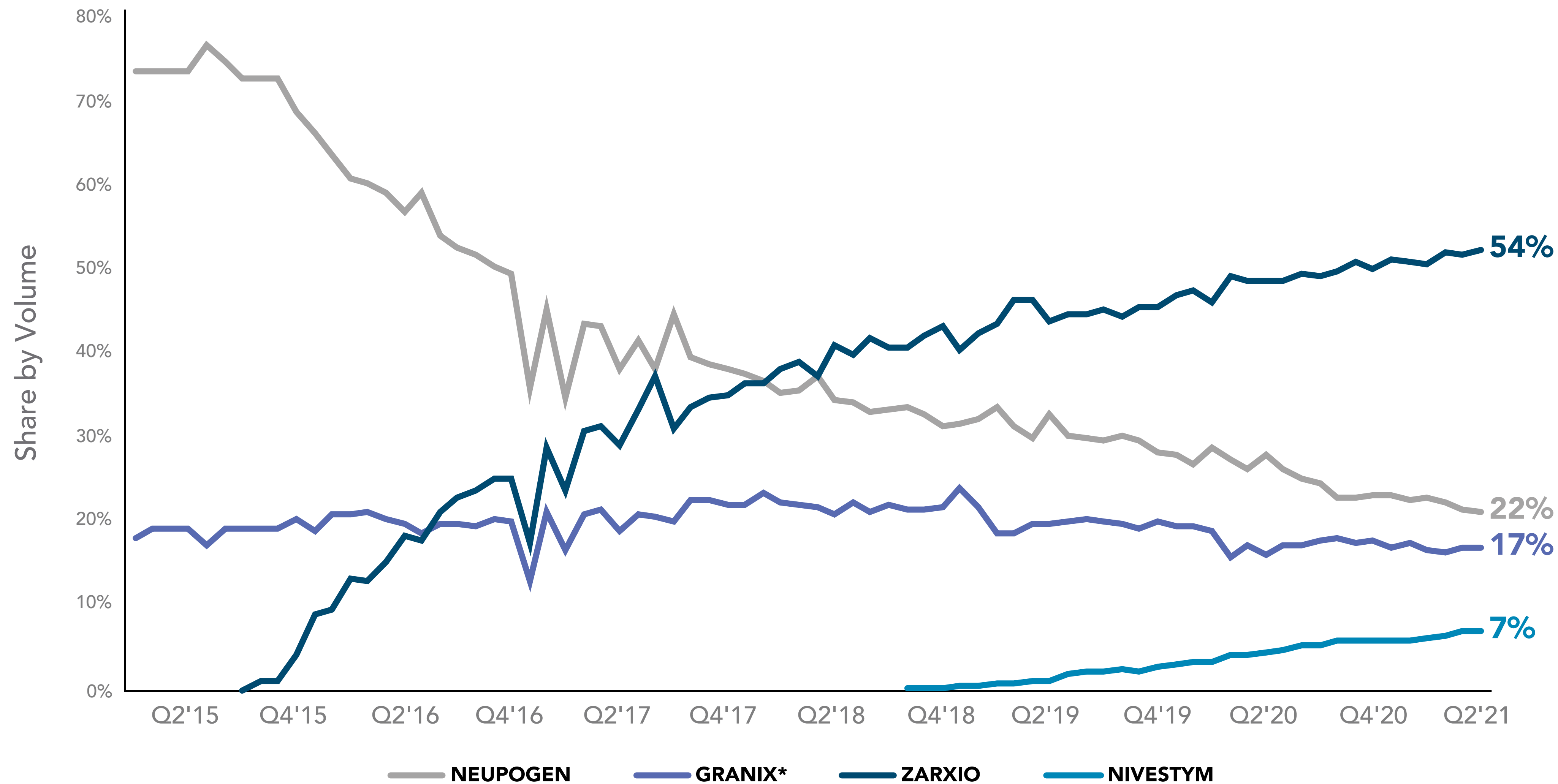


## Filgrastim

As seen in **Figure 29**, filgrastim biosimilars account for a majority of share when compared to reference product NEUPOGEN. After 2.5 years, the first filgrastim biosimilar ZARXIO captured more share than the reference product NEUPOGEN.

**As of Q2 2021, biosimilars and GRANIX account for 78% share of all filgrastim products.**

**Figure 29.** Uptake Curve for Filgrastim Products<sup>5</sup>



See **NEUPOGEN Full Prescribing Information** for complete risk information.

Key: FDA – Food and Drug Administration.  
 \*GRANIX is not a biosimilar. It was approved under a full Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.  
 Source: OBU Customer Data Pack Weekly (IQVIA DDD + Chargeback).

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# NEPHROLOGY/ONCOLOGY SUPPORTIVE CARE



For nephrology/oncology supportive care, we look at **epoetin alfa** products. We discuss:

- 1** WAC and ASP of the biosimilar at launch compared to the reference product
- 2** ASP for the reference product and biosimilars since launch
- 3** Biosimilar uptake
- 4** Estimated difference in total drug spend after biosimilar competition



*EPOGEN and PROCRIT are the same molecule; however, they are marketed by 2 different companies in separate therapeutic areas. In addition, they have independent WACs but the same ASP.*

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

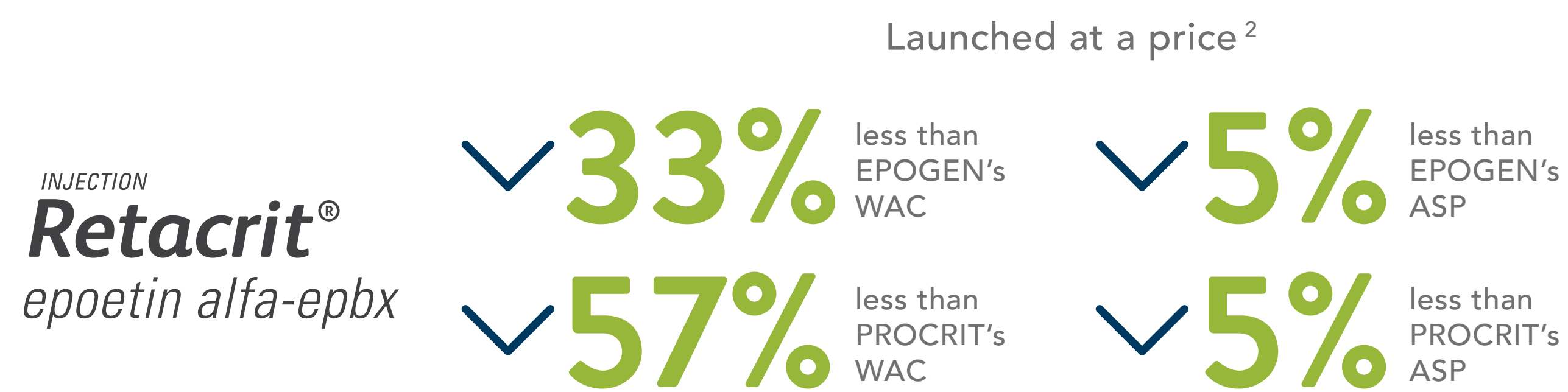
● REFERENCES

Please [click here](#) for Boxed Warning information for EPOGEN. See [Full Prescribing Information](#) for complete risk information.

# NEPHROLOGY/ONCOLOGY SUPPORTIVE CARE

## Epoetin alfa

One biosimilar has launched since 2018 to the reference products EPOGEN and PROCRIT (epoetin alfa):



● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

**Nephrology/Oncology Supportive Care**

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

Please [click here](#) for Boxed Warning information for EPOGEN.  
See [Full Prescribing Information](#) for complete risk information.

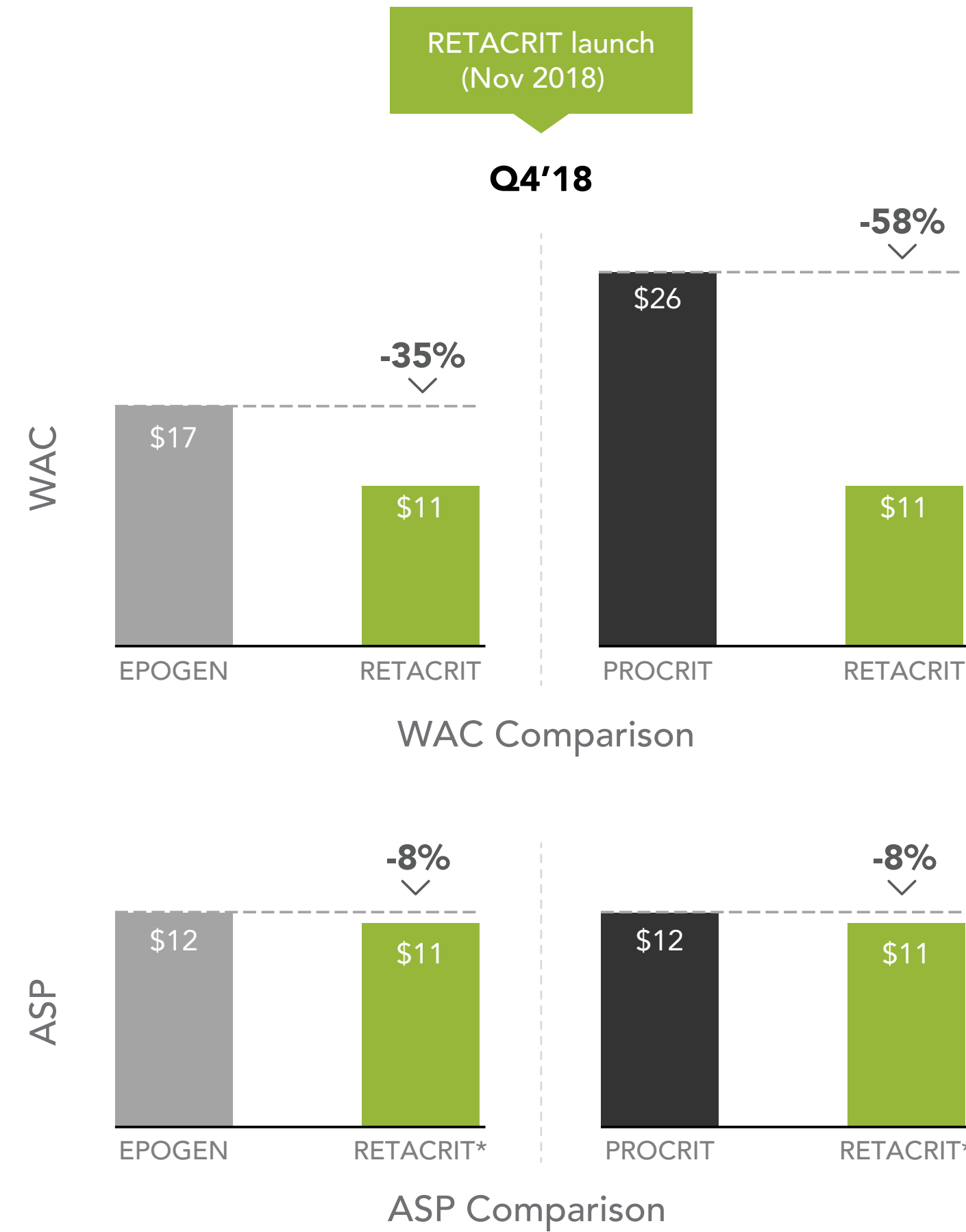
# NEPHROLOGY/ONCOLOGY SUPPORTIVE CARE



## Epoetin alfa

As **Figure 30** shows, RETACRIT launched at WAC and ASP discounts to the reference products EPOGEN and PROCRIT.

**Figure 30.** WAC and ASP of Epoetin Alfa Biosimilars Relative to Reference Products at Launch<sup>2</sup>



Please [click here](#) for Boxed Warning information for EPOGEN.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
\*ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# NEPHROLOGY/ONCOLOGY SUPPORTIVE CARE

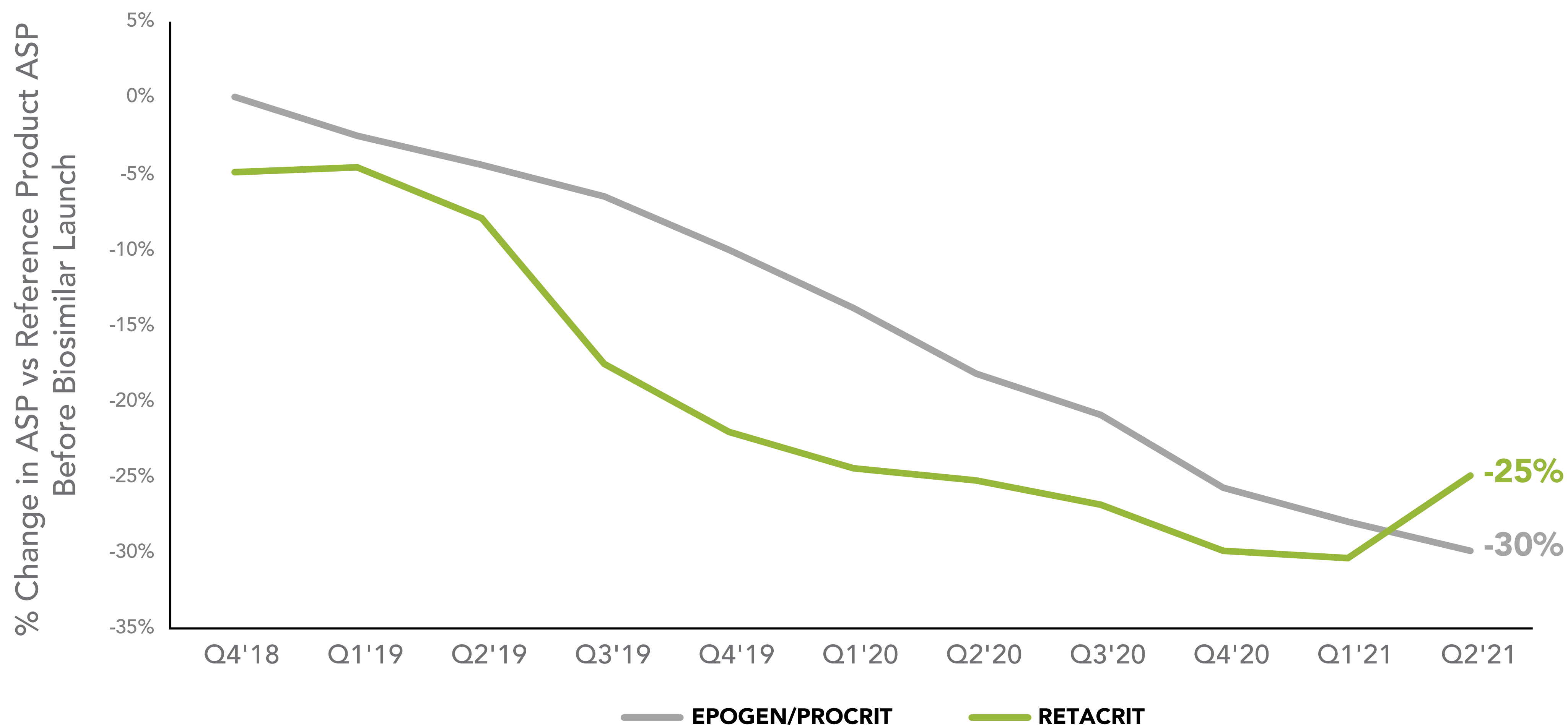


## Epoetin alfa

**Figure 31** shows the percentage change in the price of the biosimilar over time when compared to the reference products' ASP at the time that the first epoetin alfa biosimilar launched. Following the establishment of RETACRIT's ASP in April 2019, it has declined dramatically for the last 2 years until recently with an increase in Q2 2021.

**The ASP of the reference products EPOGEN and PROCRT has steadily trended downward following RETACRIT's launch.**

**Figure 31.** ASP of Epoetin Alfa Products at Biosimilars' Launch<sup>2</sup>



Please [click here](#) for Boxed Warning information for EPOGEN.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
Biosimilar WAC is used for comparing against reference product ASP until biosimilar ASP is available.  
Source: AnalySource.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES



# NEPHROLOGY/ONCOLOGY SUPPORTIVE CARE

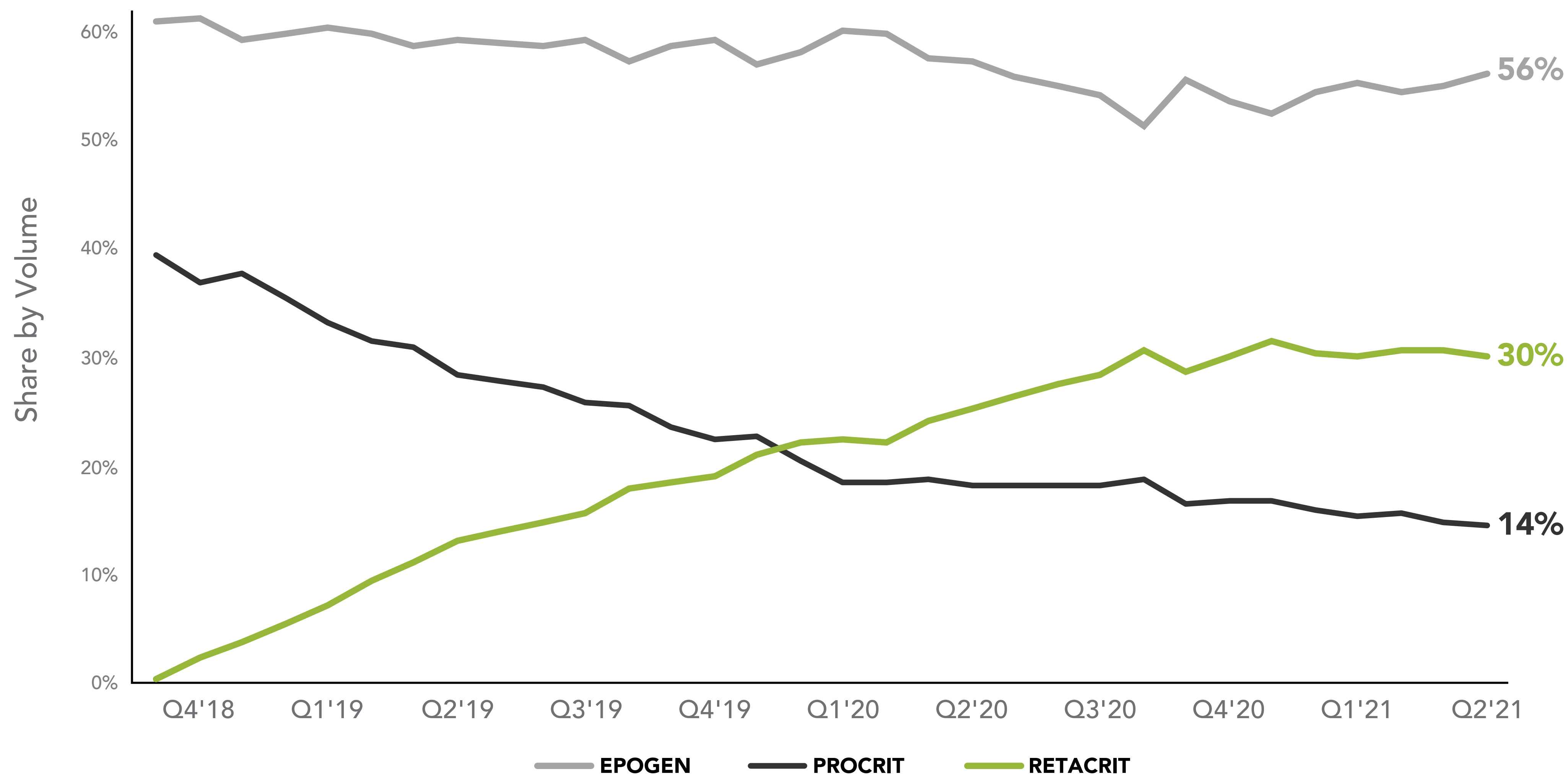


## Epoetin alfa

As seen in **Figure 32**, the epoetin alfa biosimilar RETACRIT has continued to increase its share over time, while reference products EPOGEN and PROCRIIT's share have remained relatively stable or declined, respectively. By Q1 2020 (5 quarters after its launch), the epoetin alfa biosimilar RETACRIT had captured more share than the reference product PROCRIIT.

**As of Q2 2021, RETACRIT has now captured 30% share among epoetin alfa products.**

**Figure 32.** Biosimilar Uptake Curve for Epoetin Alfa Products<sup>5</sup>



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See [Full Prescribing Information](#) for complete risk information.

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

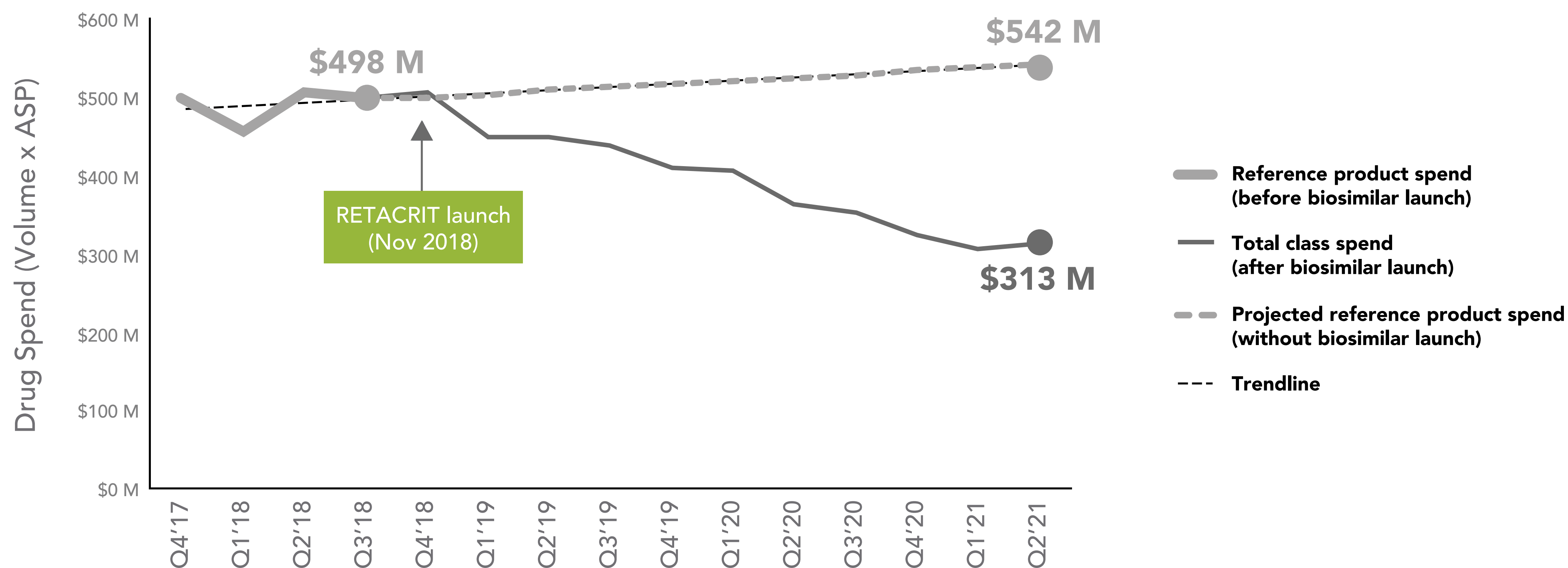
# NEPHROLOGY/ONCOLOGY SUPPORTIVE CARE

## Epoetin alfa

**Figure 33** shows the total drug spend for epoetin alfa with biosimilar launches, compared to the projected drug spend in the absence of biosimilar competition.

**The cumulative savings in drug spend for epoetin alfa from the first EPOGEN/PROCRIT biosimilar launch in Q4 2018 to Q2 2021 is estimated to be \$1.4 billion.**

**Figure 33.** Comparison of Epoetin Alfa Drug Spend With vs Without Biosimilar Competition<sup>3</sup>



Please [click here](#) for Boxed Warning information for EPOGEN.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price.  
The quarterly drug spend for each product is estimated as: Drug spend=ASPxNormalized unit volume. The estimated spend for the reference product (after biosimilar launch) is trended out based on historical spend for the reference product before biosimilar launch.  
Sources: AnalySource, Integrated Weekly Sales Data (IQVIA DDD + Chargeback).

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

# INFLAMMATION



For inflammation, we look at **infliximab** products. We discuss:

- 1** WAC and ASP of the biosimilar at launch compared to the reference product
- 2** ASP for the reference product and biosimilars since launch
- 3** Biosimilar uptake
- 4** Estimated difference in total drug spend after biosimilar competition

**Four of the 10 best-selling medicines** are anti-inflammatory biologics. Currently, **REMICADE—the fourth best-selling anti-inflammatory**—is the only product in this category with biosimilar competition in the US.<sup>15</sup>

In the next few years, patients with inflammation diseases will likely have access to more treatment options due to increasing biosimilar availability. Based on historical performance of biosimilar competition in other disease states, this should lead to cost savings.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

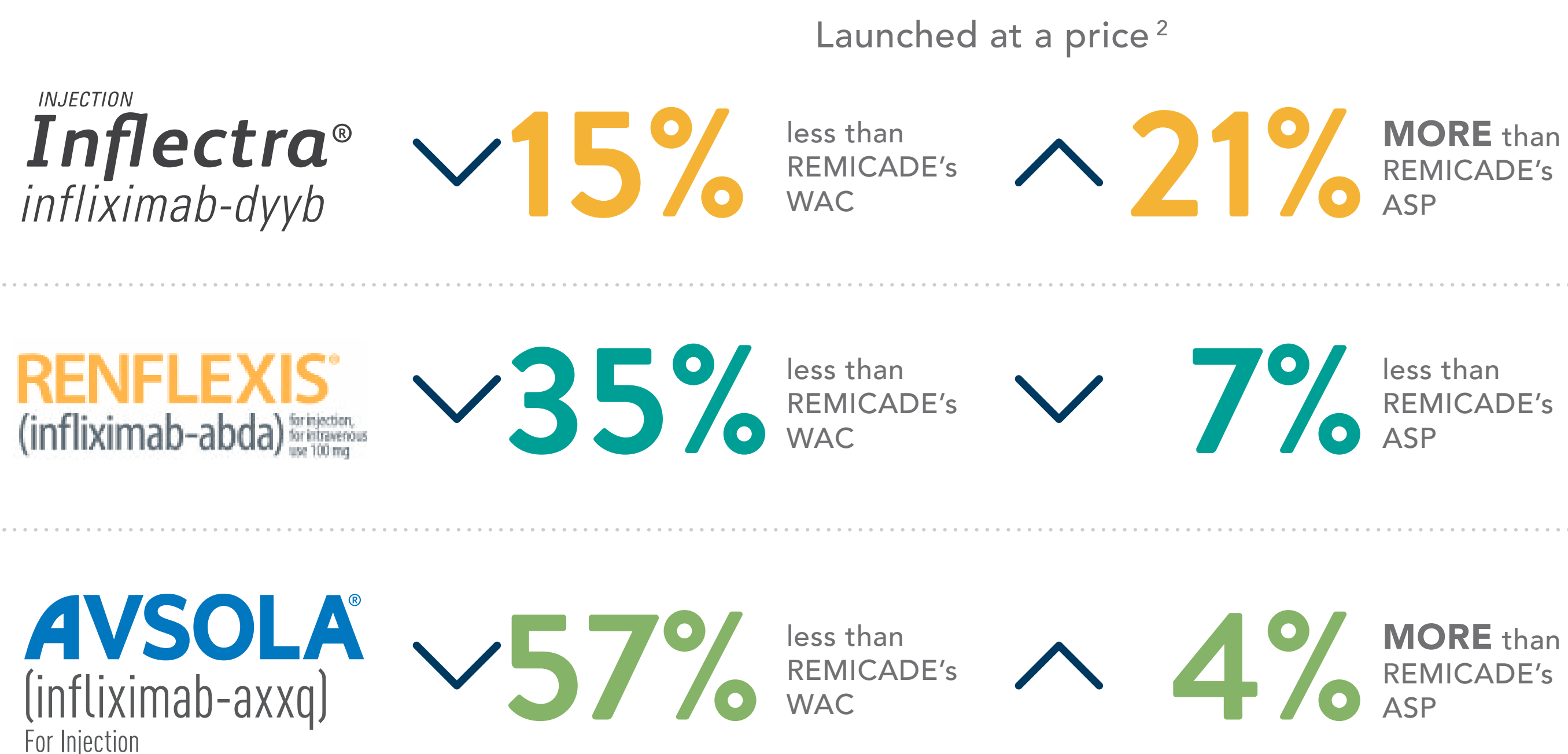
● UNDERSTANDING BIOSIMILARS

● REFERENCES

# INFLAMMATION

## Infliximab

Three biosimilars have launched—in 2016, 2017, and 2020—to the reference product REMICADE (infliximab):



Please [click here](#) for **Boxed Warning** information for AVSOLA.  
 See [Full Prescribing Information](#) for complete risk information.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

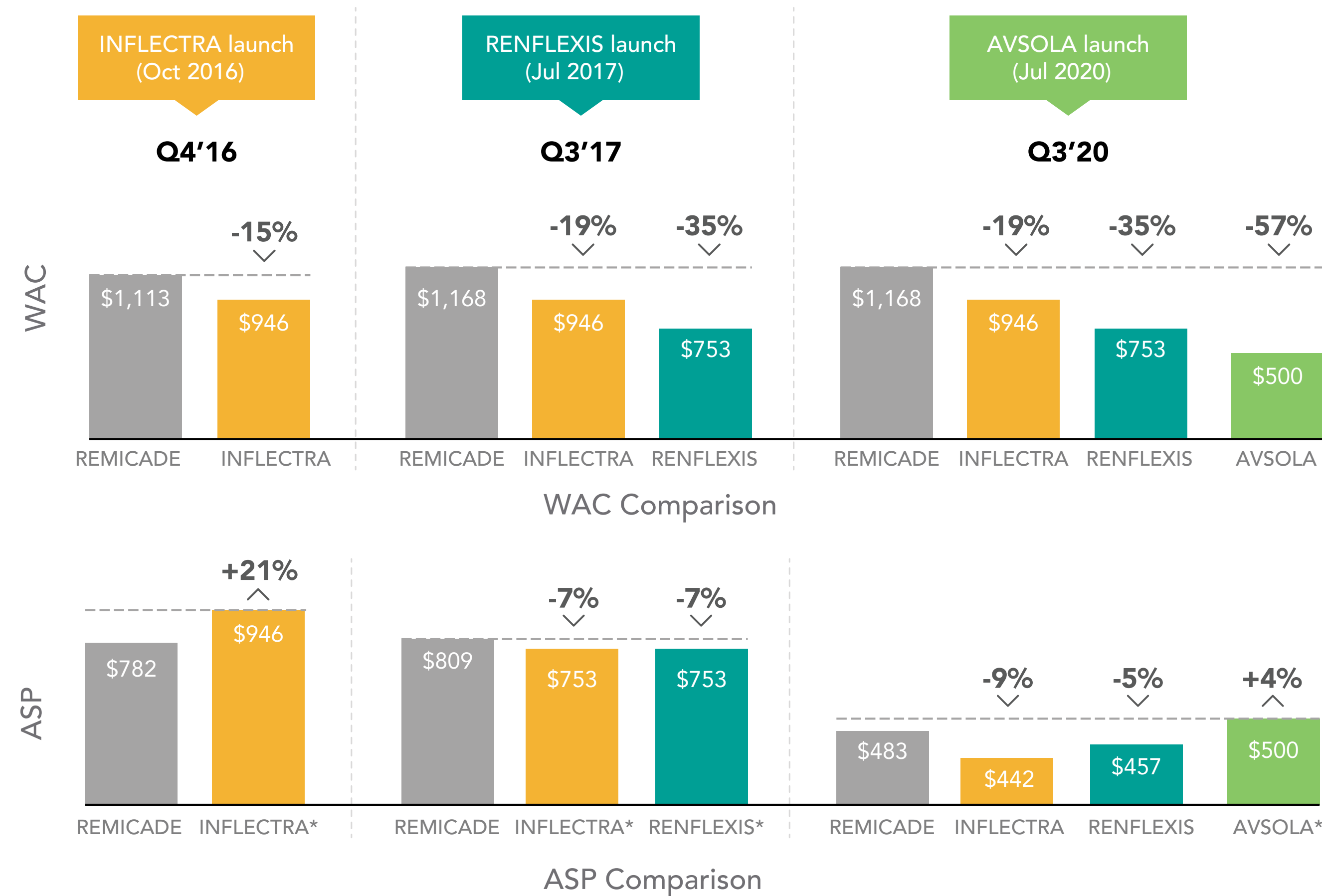
● REFERENCES

# INFLAMMATION

## Infliximab

As **Figure 34** shows, all infliximab biosimilars launched at WAC discounts to the reference product. Virtually all biosimilars in the US have launched with discounts to the reference product's ASP; however, INFLECTRA and AVSOLA launched at a premium to the reference product REMICADE's ASP. The second biosimilar, RENFLEXIS, also launched at a WAC discount to the first biosimilar, INFLECTRA, and provided WAC and ASP discounts compared with the reference product.

**Figure 34. WAC and ASP of Infliximab Biosimilars Relative to Reference Product at Launch<sup>2</sup>**



Please [click here](#) for Boxed Warning information for AVSOLA.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; US – United States; WAC – wholesale acquisition cost.  
\*ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
Source: AnalySource.



INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES

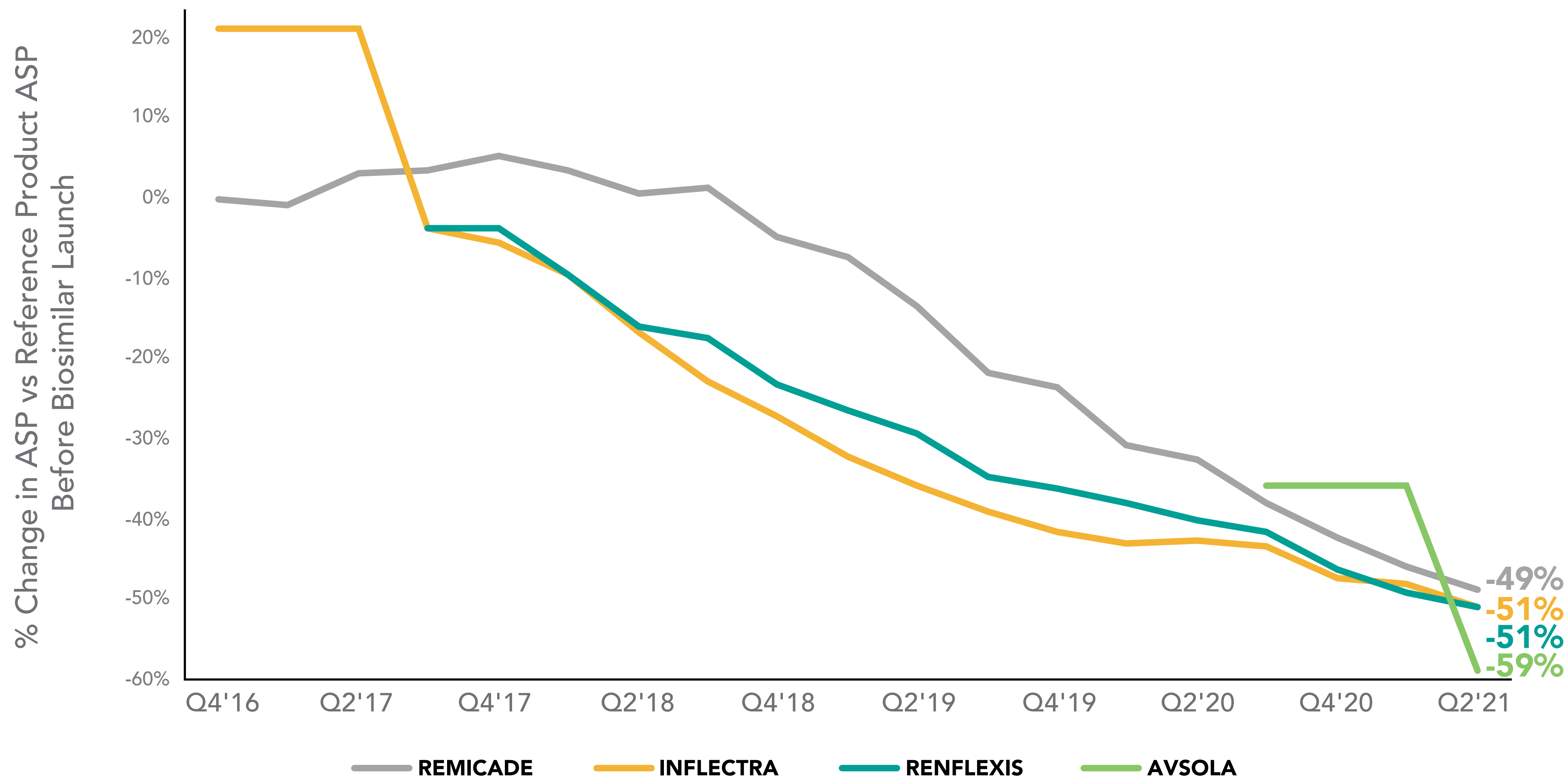
# INFLAMMATION

## Infliximab

**Figure 35** shows the percentage change in the price of biosimilars over time when compared to the reference product's ASP at the time that the first infliximab biosimilar launched. Despite launching at a premium to the reference product's ASP, INFLECTRA's price quickly declined to be lower than REMICADE once its ASP was established 3 quarters after launch.

**The ASPs for all infliximab products continued to decline after subsequent biosimilars were launched beginning in Q3 2017.**

**Figure 35.** ASP of Infliximab Products at Biosimilars' Launches<sup>2</sup>



Please [click here](#) for Boxed Warning information for AVSOLA.  
See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
Biosimilar WAC is used for comparing against reference product ASP until biosimilar ASP is available.  
Source: AnalySource.



- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

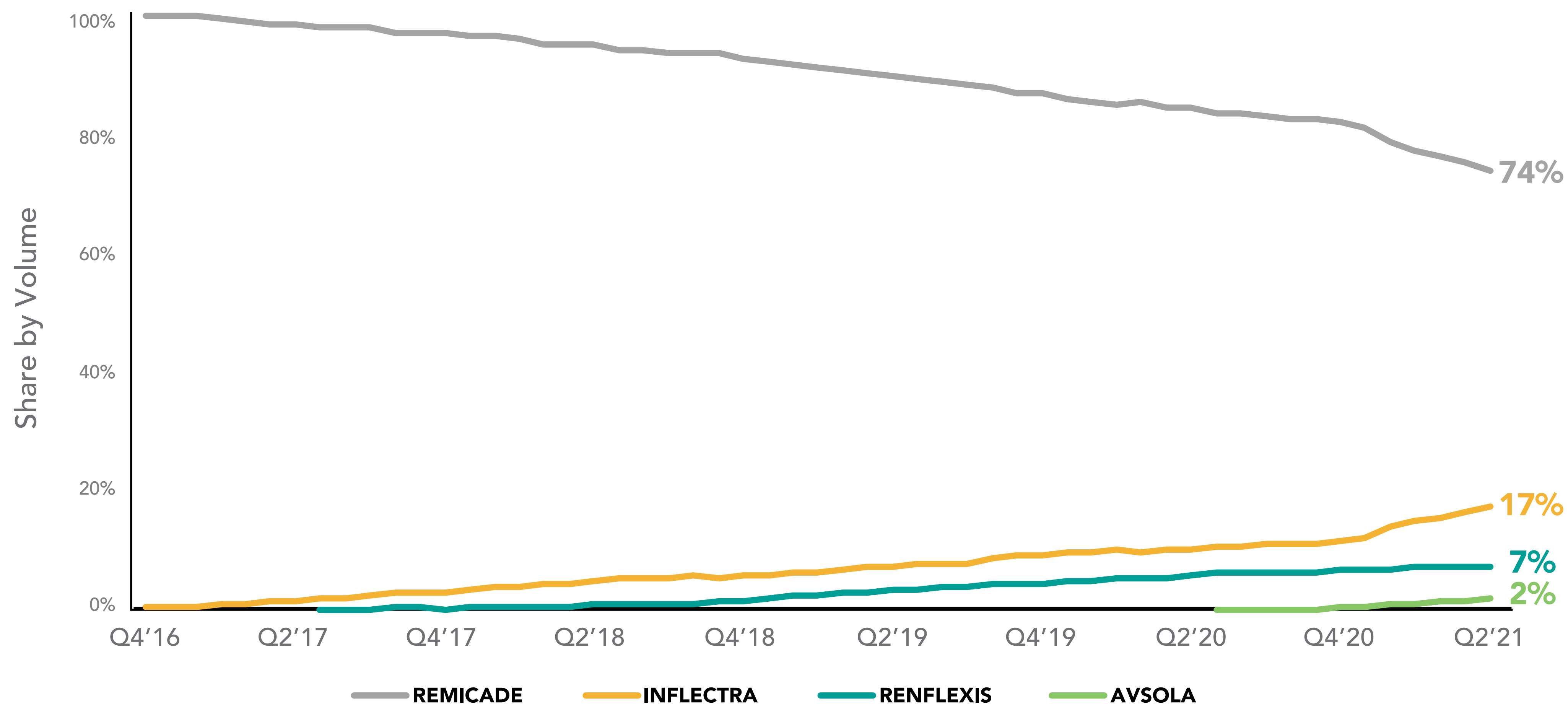
# INFLAMMATION

## Infliximab

As seen in **Figure 36**, biosimilars are beginning to capture a greater proportion of share compared to the reference product. As more biosimilars become available, reference product manufacturers are frequently willing to lower prices. Price competition from the reference product REMICADE and physician caution around changing medicines for chronic conditions like autoimmune diseases may have contributed to the slow start in capturing share for infliximab biosimilars.<sup>34,35</sup>

**After slow starts, infliximab biosimilars have gained 26% share by Q2 2021, while the reference product REMICADE has a 74% share.**

**Figure 36.** Biosimilar Uptake Curve for Infliximab Products<sup>5</sup>



Please [click here](#) for Boxed Warning information for AVSOLA. See [Full Prescribing Information](#) for complete risk information.



- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
  - Oncology Therapeutics
  - Oncology Supportive Care
  - Nephrology/Oncology Supportive Care
  - Inflammation
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

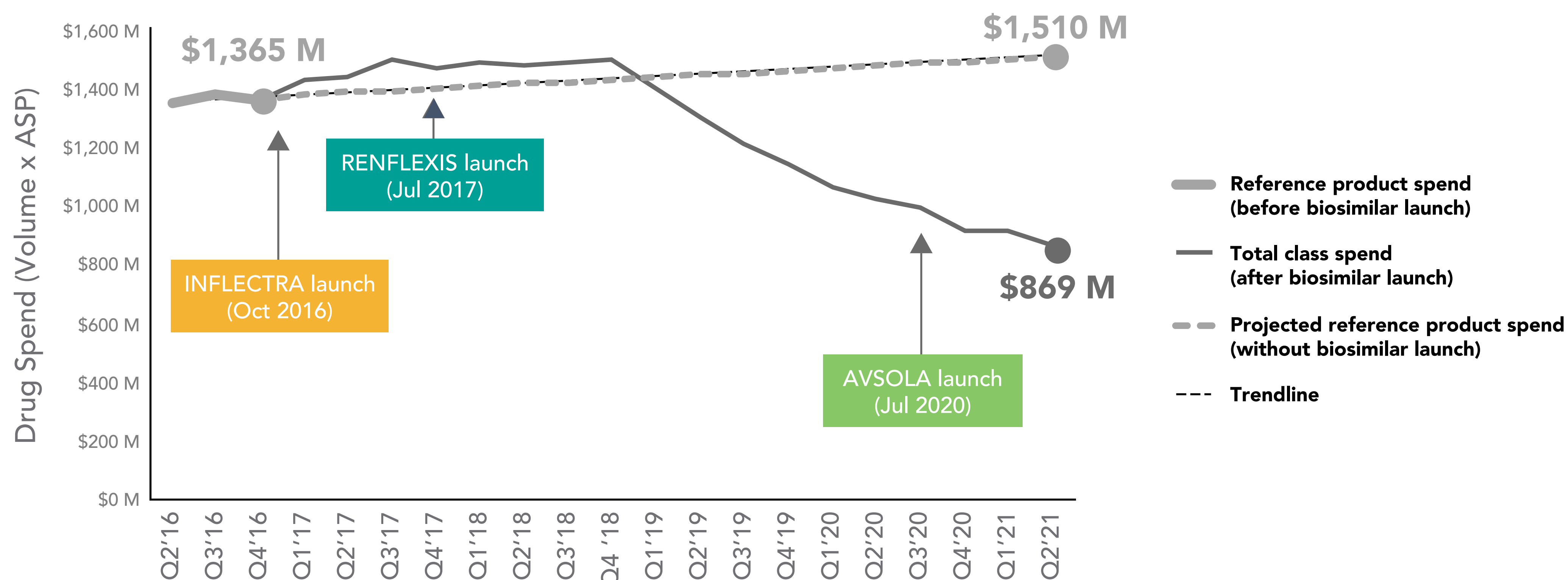
# INFLAMMATION

## Infliximab

**Figure 37** shows the total drug spend for infliximab with biosimilar launches, compared to the projected drug spend in the absence of biosimilar competition.

**The cumulative savings in drug spend for infliximab from Q4 2016 to Q2 2021 is estimated to be \$3.3 billion.**

**Figure 37. Comparison of Infliximab Drug Spend With vs Without Biosimilar Competition<sup>3</sup>**



Please [click here](#) for Boxed Warning information for AVSOLA. See [Full Prescribing Information](#) for complete risk information.

Key: ASP – average sales price. The quarterly drug spend for each product is estimated as: Drug spend=ASPxNormalized unit volume. The estimated spend for the reference product (after biosimilar launch) is trended out based on historical spend for the reference product before biosimilar launch. Sources: AnalySource, Integrated Weekly Sales Data (IQVIA DDD + Chargeback).

INTRODUCTION AND REPORT OVERVIEW

CURRENT STATE OF THE MARKETPLACE

FUTURE STATE OF THE MARKETPLACE

TRENDS

Oncology Therapeutics

Oncology Supportive Care

Nephrology/Oncology Supportive Care

Inflammation

STAKEHOLDER CONSIDERATIONS

REIMBURSEMENT

POLICY UPDATE

UNDERSTANDING BIOSIMILARS

REFERENCES



# STAKEHOLDER CONSIDERATIONS

- > Healthcare Systems
- > Providers
- > Payers and Employers
- > Patients

● INTRODUCTION AND  
REPORT OVERVIEW

● CURRENT STATE OF  
THE MARKETPLACE

● FUTURE STATE OF  
THE MARKETPLACE

● TRENDS

● **STAKEHOLDER  
CONSIDERATIONS**

Healthcare Systems

Providers

Payers & Employers

Patients

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING  
BIOSIMILARS

● REFERENCES



# HEALTHCARE SYSTEMS

## Potential benefits to society, payers, providers, and patients

Biosimilars offer potential benefits to every stakeholder in the healthcare system. They may lower spending by offering a potentially lower-cost treatment option. Also, competition fostered by the introduction of biosimilars may lead to savings that can be redeployed toward spending on new, innovative therapies.

Compared to the reference products, biosimilars may create opportunities to lower spending for payers, employers, state and federal governments, and patients.<sup>36</sup> Two factors – the abbreviated approval pathway and the creation of competition – can primarily drive these savings:



### Developing a biosimilar costs less than a reference biologic because of the abbreviated FDA approval pathway

Biosimilars are expected to **cost between \$124 million and \$248 million** (adjusted to 2021 dollars) to develop compared to an estimate of \$2.6 billion for developing a new drug or biologic.<sup>37-40</sup> As a result, manufacturers have fewer expenses to recoup, which theoretically contributes to the possibility of biosimilars having lower list prices.



### Biosimilars contribute to competition in the healthcare system

As the number of treatment choices increases for a particular disease or condition, **manufacturers may be incentivized to lower the prices of their products** to remain competitive.<sup>36</sup>

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- **STAKEHOLDER CONSIDERATIONS**
  - Healthcare Systems
  - Providers
  - Payers & Employers
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# PROVIDERS



Healthcare professionals, including physicians, physician assistants, nurse practitioners, and pharmacists, are central to the adoption of biosimilars.

Healthcare professionals:



**Have confidence in the evidence and the approval process, and physicians specifically have the confidence to prescribe and use biosimilars**



**Ensure that their practices have operational processes in place to prepare for use of biosimilars**



**Have confidence that biosimilars are covered by payers and are reimbursed in a timely fashion**



**Have a central role in educating patients and ensuring biosimilars can be appropriately used in everyday clinical practice**

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- **STAKEHOLDER CONSIDERATIONS**
  - Healthcare Systems
  - Providers**
  - Payers & Employers
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES



# PROVIDERS

## Educational campaigns

Science-based education about biosimilars may provide stakeholders with greater confidence in their use. Educational campaigns by the FDA and organizations such as the Biologics Prescribers Collaborative (BPC), American Society of Clinical Oncology (ASCO), Community Oncology Alliance (COA), Pharmaceutical Research and Manufacturers of America (PhRMA), and Biotechnology Innovation Organization (BIO) include:



Scientific information about the complexity of manufacturing biologics, including biosimilars



The concept of extrapolation



How biosimilars are approved by regulators



Clinical considerations for use

Specialty societies of physicians, nurse practitioners, and others are recognizing the promise of biosimilars for providers and patients, so these groups have been placing increasing importance over the last few years on educating their members about biosimilars.<sup>41,42</sup>



### CANCER:

In October 2020, ASCO published an update to its guideline on treating early-stage breast cancer, in which it endorsed the use of biosimilar trastuzumab.<sup>43</sup> Additionally, in 2019, COA released a position statement saying it will work with stakeholders to support the acceptance of biosimilars by educating oncologists.<sup>44</sup>



### RARE DISEASES:

Since 2019, the rare-disease patient and provider community has supported a common set of principles to promote the use of biosimilars.<sup>45</sup>



### Why should manufacturers have a sales force?

It is important for manufacturers to support their biosimilar products with a capable sales force. Despite providers' growing familiarity with biosimilars, **there are still knowledge gaps related to biosimilars** among all participants in the healthcare system, including patients, payers, pharmacists, and healthcare professionals. **A well-prepared sales force can help address those knowledge gaps.**

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- **STAKEHOLDER CONSIDERATIONS**
  - Healthcare Systems
  - Providers**
  - Payers & Employers
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

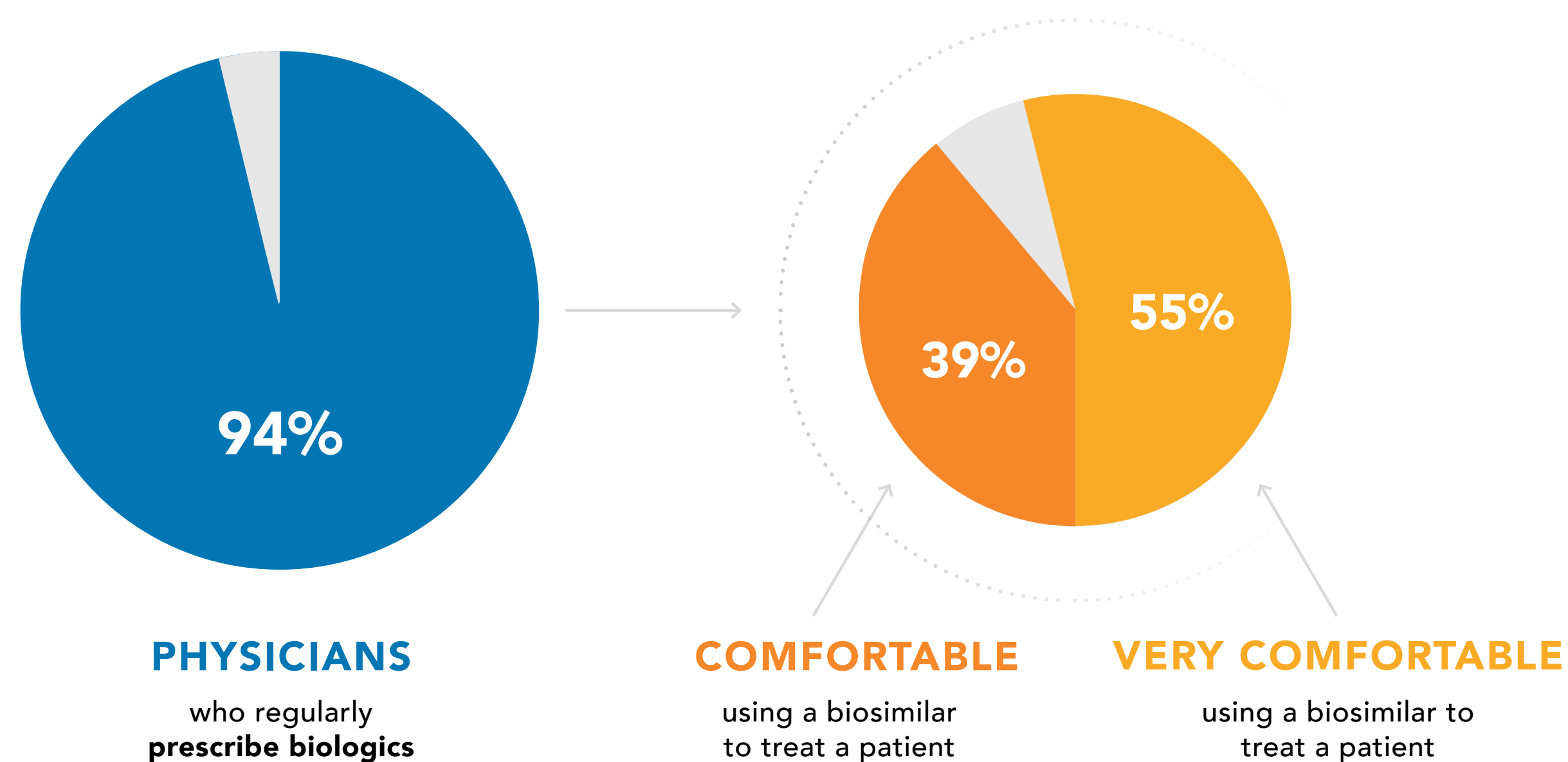
# PROVIDERS

## Biosimilar awareness

**Providers are becoming increasingly familiar with prescribing biosimilars; however, there remains work to be done.**

Seven years after the first biosimilar launched in the US, physician knowledge of biosimilars in each specialty where they are available continues to grow. Providers are becoming increasingly familiar with prescribing biosimilars; however, there are still knowledge gaps to be filled, such as perceptions of prescribing physicians about the safety of biosimilars and confidence around switching from a reference product to a biosimilar.<sup>46</sup>

**A recent survey of 602 specialists who regularly prescribe biologics, conducted by the National Opinion Research Center (NORC) at the University of Chicago, found that 94% of physicians were either very comfortable (55%) or comfortable (39%) with using a biosimilar to treat a patient.<sup>47</sup>**



**“It is about becoming comfortable with the concept that [biosimilars] are therapeutically equivalent [to the originator].”<sup>48</sup>**

– Angus Worthing, MD,  
Georgetown University Medical Center

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
  - Healthcare Systems
  - Providers
  - Payers & Employers
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# PROVIDERS

## Operational processes

Savings expected from biosimilars are particularly important when considering that hospital systems and provider groups are focused on providing consistent quality care to their patients while being mindful of costs and potential savings opportunities.

Health systems and providers will need to prepare for the growing availability of biosimilars by <sup>49</sup>:

 **Anticipating potential differences in delivery device between a reference product and a biosimilar**

 **Understanding differences in electronic health record tracking when stocking the reference product and biosimilar**

 **Being familiar with major payers' coverage and reimbursement policies for biosimilars**

 **Understanding the different patient support services provided by biosimilar manufacturers**

To maximize the benefit when a payer covers a biosimilar, providers will need **ongoing education**, may need **operational changes**, and might even need to become **internal champions**.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● **STAKEHOLDER CONSIDERATIONS**

Healthcare Systems

Providers

Payers & Employers

Patients

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES

# PROVIDERS

## Case study: Strategies for biosimilar implementation

Beginning in late 2019, West Cancer Center (WCC) began formally adopting commercially available biosimilars. Between September 2019 and June 2020, WCC tracked utilization data from 2 reference products and their biosimilars, as well as provider perspectives throughout the adoption process.

**Key factors identified by WCC for successful biosimilar adoption are <sup>50</sup>:**

**Clinical leadership and decision making** to incorporate biosimilars into care pathways and intervene when adoption rates are low

**Electronic medical record integration** to streamline adoption, understand practice patterns, and facilitate reporting

**Formulary operations and inventory management** to provide a seamless point-of-care experience

**Biosimilar education for clinical staff and patients** to ensure a smoother adoption of biosimilars



**WEST**  
CANCER CENTER  
& RESEARCH INSTITUTE

**West Cancer Center is an adult cancer care and research center serving more than 40,000 patients annually at 9 sites in the southern US.**



To read the full WCC biosimilar implementation case study published in the *American Journal of Managed Care* in December 2020, [click here](#).

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
  - Healthcare Systems
  - Providers
  - Payers & Employers
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

## High-quality, reliable supply

The FDA holds all biologics – both reference products and biosimilars – to the same Good Manufacturing Practice standards.<sup>51</sup> Biosimilar manufacturers must have a long-term commitment to quality for biosimilars to succeed. When choosing a biosimilar, providers may want to consider manufacturers’ dedicated experience manufacturing biosimilars, and biologics in general.

Providers should consider a manufacturer’s history of shortages and recalls and evaluate its capability to maintain adequate production and stock to support demand when deciding to use any product. Providers should also consider the robustness of the manufacturer’s supply chain when evaluating product use.<sup>52</sup>

# PAYERS AND EMPLOYERS

## Payers

Payers are looking to biosimilars as an opportunity to help manage costs and offer more treatment choices.<sup>53</sup> The availability of biosimilars in key therapeutic categories that currently have only 1 or a few reference products available promotes competition and is a tool payers and other stakeholders may use to help lower costs.

**Payers must evaluate several clinical, economic, and manufacturer partner factors when considering adding biosimilars to the formulary, including<sup>53</sup>:**



Robust regulatory standards to demonstrate biosimilarity



How biosimilars will be covered, placed on formularies, and utilization management mechanisms



Whether providers will be willing to prescribe them



Whether, how, and when to switch patients to biosimilars



Their potential to decrease costs while maintaining patient access to necessary treatments



Cost-effectiveness



Manufacturer experience with biologics in the therapeutic area



Manufacturer ability to supply reliably



Manufacturer past performance with biosimilars

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● **STAKEHOLDER CONSIDERATIONS**

Healthcare Systems

Providers

**Payers & Employers**

Patients

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



# PAYERS AND EMPLOYERS

## Payer adoption of biosimilars

**Biosimilars offer the potential of cost savings to payers for both the reference product and the biosimilar.**

Increasingly, payers are showing a desire to embrace biosimilars, which could help promote competition and potentially lower costs for the US healthcare system.

One study estimated that gradually shifting patients to a ZIRABEV (bevacizumab) biosimilar would provide **substantial cost savings** for US payers.<sup>54</sup>

**Several examples from recent years show how payers are acknowledging the value of biosimilars in lowering healthcare costs and driving savings:**

In July 2021, **Cigna** announced that 2 biosimilars for REMICADE (infliximab), AVSOLA and INFLECTRA, will move to preferred status.

Cigna acknowledged that, with the formulary change, it is

**“taking concrete steps to help patients and plans realize the promise of alternative, clinically effective treatment options.”<sup>55</sup>**

– Dr. Steven Miller  
Chief Clinical Officer, Cigna

In October 2020, **UnitedHealthcare (UHC)** updated its Specialty Medical Injectable Drug Program to state:

**“Biosimilars create a more competitive pricing environment among drug manufacturers that can help drive down drug costs and the continued development of new biosimilar medications is a key factor in long-term specialty cost management. [UHC] strives to provide coverage for biosimilars whenever possible to ensure a robust pipeline of future products.”<sup>56</sup>**

– UnitedHealthcare Specialty Medical Injectable Drug Program Updates, 2020

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- **STAKEHOLDER CONSIDERATIONS**
  - Healthcare Systems
  - Providers
  - Payers & Employers**
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# PAYERS AND EMPLOYERS

## Employers

With 158 million people (50% of the US population) covered by employer-sponsored insurance, employers have a vested interest in controlling and containing healthcare costs.<sup>57</sup> Biosimilars are a potential path forward to reduce costs for employees, who are absorbing a greater percentage of healthcare costs each year.

Escalating healthcare costs, historically low interest rates, and an aging workforce have made employee benefits a significant budget line item for employers over the last 10 years. Large companies estimate that their total cost of healthcare, including premiums and out-of-pocket costs for employees and dependents, will increase 5.3% in 2021.<sup>58</sup>

## Biosimilar adoption and impact for employers

Escalating specialty drug costs present a challenge for many employers trying to control their healthcare spend while maintaining a profitable business. Continued biosimilar penetration could help increase competition and lower costs without compromising quality, efficacy, or patient safety. One strategy to lower employers' cost burden is the integration of value-based policies to help navigate the challenges of rebates, provider incentives, and provider education of biosimilars.<sup>59</sup>

A 2020 study examined the impact of biosimilars on the health benefits spending of multiple large employers. The study focused on claims data for filgrastim and infliximab.<sup>60</sup>



Patients who took the biosimilar paid on average 12% (~\$300) and 45% (~\$600) less out of pocket per year than those who took the reference product (infliximab and filgrastim, respectively)



These savings were primarily due to a combination of lower frequency of coinsurance requirements and lower biosimilar list prices compared to beneficiaries taking the reference biologic

The 24th annual Best Practices in Health Care Employer Survey by Willis Towers Watson found **30% of employers** have created incentives and requirements to promote the use of biosimilars in their formulary or plan design, and another **39% of employers** plan to explore this strategy in the next 2 years.<sup>61</sup>

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
  - Healthcare Systems
  - Providers
  - Payers & Employers**
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# PAYERS AND EMPLOYERS

## Biosimilar adoption and impact for employers

**Biosimilars offer employers an opportunity to lower their growing health costs.**

The National Alliance of Healthcare Purchaser Coalitions provided steps for employers to “influence change that will ultimately lead to more options for employees and their dependents who are dealing with diseases like cancer, rheumatoid arthritis, inflammatory bowel disease, diabetes, multiple sclerosis, kidney disease, and severe psoriasis” <sup>62</sup>:



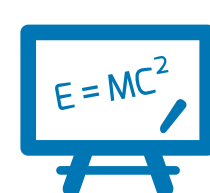
Quantify the biosimilar opportunity by initiating conversations with vendors about fill rates and savings potential



Partner with vendors to determine how best to drive appropriate promotion, adoption, and utilization of biosimilars



Review specialty pharmacy benefit design to ensure that it supports appropriate use and access to biosimilars



Educate all employees about the value of biosimilars to enable more informed decision making

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- **STAKEHOLDER CONSIDERATIONS**
  - Healthcare Systems
  - Providers
  - Payers & Employers**
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# PATIENTS



**Educating patients about biosimilars will be a crucial part of their comfort level with the products.**

Patient understanding of biosimilar products, including their safety and efficacy, will be key to the utilization of these drugs. Education on what biosimilars are and the potential for cost savings will be of paramount importance to encourage their utilization.<sup>63</sup>

It is important for patients to understand the following:

 **What is a biosimilar? Is it safe and effective?**

 **Do biosimilars undergo the same development process as other FDA-approved products?**

 **How much will a biosimilar cost me? Are there patient assistance programs for biosimilars to help me with these costs?**

 **Is there an FDA-approved biosimilar for the biologic I'm taking? Is it appropriate me being switched to it?**

 **How many other patients like me have been treated with a biosimilar to the product I'm currently taking?**

The ability of biosimilars to lower patients' out-of-pocket costs has real potential. A 2020 analysis estimated the potential out-of-pocket savings opportunity across the 9 biologic medicines where biosimilar competitors have been approved. The results demonstrate clear opportunities for biosimilars to lower patients' costs<sup>4</sup>:



Depending on the drug, and based on the treatment assumptions, biosimilars can reduce patients' out-of-pocket costs by up to 47% per year



Biosimilars can reduce total out-of-pocket spending by \$238 million for patients in just the 9 biologic drug classes where biosimilars have been approved



[Click here](#) to see the patient resources available on the FDA's website.

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
  - Healthcare Systems
  - Providers
  - Payers & Employers
  - Patients
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# REIMBURSEMENT

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- **REIMBURSEMENT**
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# MEDICARE UPDATES



As of January 2018, CMS assigns each biosimilar a unique payment code (known as a HCPCS code), and its ASP is not combined with other biosimilars of the same reference product.<sup>7</sup>

Assigning a unique HCPCS code to each biosimilar can help promote a robust, competitive landscape by:



Increasing the potential for innovation



Allowing each product to be treated on its own for reimbursement purposes. Distinct HCPCS codes additionally reduce potential for confusion for traceability that would be created by shared codes.



Lowering risks associated with developing and marketing these complex products



Helping physicians have certainty around their reimbursement rate if they choose a different biosimilar of the same reference product

Please refer to the [Understanding Biosimilars](#) section at the end of the report for coding, coverage, and payment characteristics of biosimilars among various payers.

The Affordable Care Act (ACA) included language to promote a level playing field between reference products and biosimilars. As shown in **Figure 38**, Medicare Part B reimburses providers for biosimilars at the biosimilar's ASP plus a 6% add-on of the reference biologic's ASP.\*<sup>7</sup> In other words, Congress kept the field level by providing physicians the same add-on amount regardless of whether they prescribe a reference product or a biosimilar. This helps all manufacturers to compete on equal terms.

**Figure 38. Medicare Part B Reimbursement for Biosimilars<sup>7</sup>**



Part B Payment for Biosimilars = Biosimilar ASP + 6% of reference biologic's ASP



**Important: Congress and the president have suspended the sequester, including the 2% mandatory payment reduction for the Medicare program, from May 1, 2020, through December 31, 2021.<sup>64</sup> Sequestration is scheduled to resume January 1, 2022.<sup>65</sup>**

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

Key: ASP – average sales price; CMS – Centers for Medicare & Medicaid Services; HCPCS – Healthcare Common Procedure Coding System.

\*Sequestration is a statutory 2% payment reduction across all Medicare spending, established under the Balanced Budget and Emergency Deficit Control Act of 1985.<sup>66</sup> Sequestration has been suspended through December 31, 2021.<sup>65</sup> When it resumes, the ASP add-on amount will be 4.3% (not 6%).

# MEDICARE UPDATES



Because there is often a lag time of 2 calendar quarters from the time when a product launches until its ASP is published, Medicare reimburses Part B drugs – including biosimilars – based on their WAC plus a 3% add-on until the ASP becomes available. Once ASP data are available, Medicare reimburses biosimilars using the ASP methodology (ASP plus 6% of the reference product’s ASP).<sup>14</sup>

**Table 3** shows hypothetical examples of physician office or community clinic and outpatient payments for a biosimilar under Medicare Part B.

**Table 3.** Payment Methodology for Biosimilars Under Medicare Part B

Biologic product	Reference product	Biosimilar A	Biosimilar B
WAC (list price)	<b>\$1,000.00</b>	<b>\$800.00</b>	<b>\$700.00</b>
ASP*	\$800.00	\$640.00	\$560.00
6% of reference product’s ASP		\$48.00	
Payment rate (ASP + 6%)	\$848.00	\$688.00	\$608.00
Patient cost-share (20%)	\$169.60	\$137.60	\$121.60

Note: Payment rate does not reflect sequester reductions.

Key: ASP – average sales price; WAC – wholesale acquisition cost.  
 \*Note: This hypothetical example assumes that the biologics’ (both reference and biosimilar) ASPs are 20% less than the WAC based on rebates over time.

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# 340B PROGRAM



The 340B Drug Pricing Program requires pharmaceutical manufacturers participating in Medicaid to sell outpatient drugs at discounted prices to nonprofit healthcare organizations that provide care for many uninsured and low-income patients. Sites within a healthcare system that qualify as 340B entities can obtain federally mandated “ceiling price” discounts for covered outpatient drugs. <sup>67</sup>

Before January 1, 2018, Medicare paid both 340B and non-340B hospitals at the same rate for certain 340B treatments, such as biologics (including biosimilars), even though 340B hospitals can obtain those treatments at a discount. <sup>68</sup> Effective January 1, 2018, however, Medicare pays for non-pass-through drugs and biologics (other than vaccines) purchased through the 340B program at ASP minus 22.5%. <sup>7</sup> As of publication, CMS finalized plans to continue to pay ASP minus 22.5% for 340B-acquired drugs through calendar year 2021. However, the agency acknowledged it would “continue to consider the appropriateness of using 340B hospital survey data to set future payment rates for 340B drugs.” While this has no impact on 2021, CMS may use hospital survey data to determine future payment rates for 340B drugs. <sup>69</sup>

## Ongoing Story

**In 2018 and 2019, CMS instituted a nearly 30% payment reduction to 340B drugs by changing their reimbursement rate from ASP plus 6% to ASP minus 22.5%.** After a challenge to the payment policy was filed, the policy was ultimately upheld by a US district court in July 2020. <sup>70</sup>

**340B healthcare organizations include nonprofit community health centers, children’s hospitals, hemophilia treatment centers, critical access hospitals, sole community hospitals, rural referral centers, and public and nonprofit disproportionate-share hospitals that serve low-income and indigent populations. <sup>71</sup>**

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES



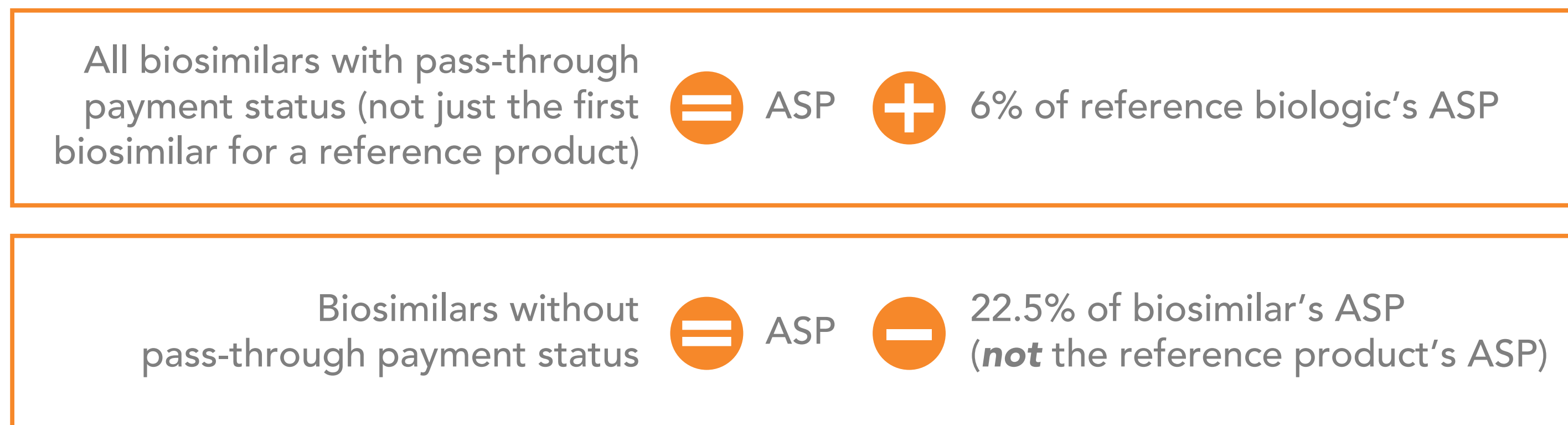
# 340B PROGRAM



The Medicare payment amounts for products under the 340B program change depending on the product's pass-through payment status. For non-pass-through biosimilars purchased through the 340B program, CMS will continue its policy of paying ASP minus 22.5% of the biosimilar's ASP.<sup>72</sup>

For calendar year 2021, CMS continues its current policy to make all biosimilars eligible for pass-through payment, not just the first biosimilar for a reference product. Additionally, CMS continued its policy that any biosimilar with pass-through payment status will be exempt from Medicare's alternative payment methodology for 340B drugs (ie, ASP minus 22.5%).<sup>73</sup> **Table 4** shows an example of a comparison of reference biologic and biosimilar Part B reimbursement in the hospital outpatient department.<sup>74</sup>

## Medicare reimbursement for biosimilars under the 340B program



It is helpful for decision makers in hospitals and health systems to be aware of any differences between a biosimilar and its reference product, as well as biosimilars with and without **pass-through payment status**, with respect to the 340B program.

**Table 4.** Hospital Outpatient Department Payment Methodology for 340B Reference Biologics and 340B Biosimilars in Medicare Part B\*<sup>74</sup>

Biologic product	Reference product	Biosimilar A, <u>with</u> pass-through status	Biosimilar A, <u>without</u> pass-through status
WAC (list price)	\$1,000.00	\$800.00	\$800.00
ASP <sup>†</sup>	\$800.00	\$640.00	\$640.00
6% of reference product's ASP	N/A	\$48.00	N/A
22.5% of its own ASP	\$180.00	N/A	\$144.00
Hospital outpatient payment rate	\$620.00	\$688.00	\$496.00
Patient cost-share (20%)	\$124.00	\$137.60	\$99.20

Key: ASP – average sales price; CMS – Centers for Medicare & Medicaid Services; N/A – not applicable; WAC – wholesale acquisition cost.  
 \*Please note that sequestration has been suspended through December 31, 2021, and is scheduled to resume January 1, 2022.  
<sup>†</sup>Note: This hypothetical example assumes that the biologics' (both reference and biosimilar) ASPs are 20% less than the WAC based on rebates over time.

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# POLICY UPDATE

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- **POLICY UPDATE**
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# BIOSIMILARS POLICY OVERVIEW



The COVID-19 pandemic has strained healthcare resources, and many patients were impacted by a loss of wages or employer-provided health insurance that hindered their ability to bear out-of-pocket costs for healthcare services and medications. Overall, the United Nations estimated the pandemic cost the global economy around \$2 trillion in 2020.<sup>75</sup>

With policymakers focused on alleviating cost pressures in the face of external crises, biosimilars may play an important role in achieving that goal. Competition created by reliably supplied, high-quality biosimilars has the potential to alleviate some of the financial burden for governments, hospitals, and patients while delivering the clinical benefits of biologic medicines.

With this in mind, certain US federal policy changes have been made to ensure a level playing field between reference products and biosimilars, which will allow physicians to choose which product is best for their patients. Recently, the debate has shifted to examining policies that tilt that competitive field to give certain coverage and payment advantages to biosimilars.<sup>76</sup> While well-intended, the debate in Congress over policy proposals that would incentivize biosimilar utilization must be sure not to compromise free market price competition or stifle innovation and growth.

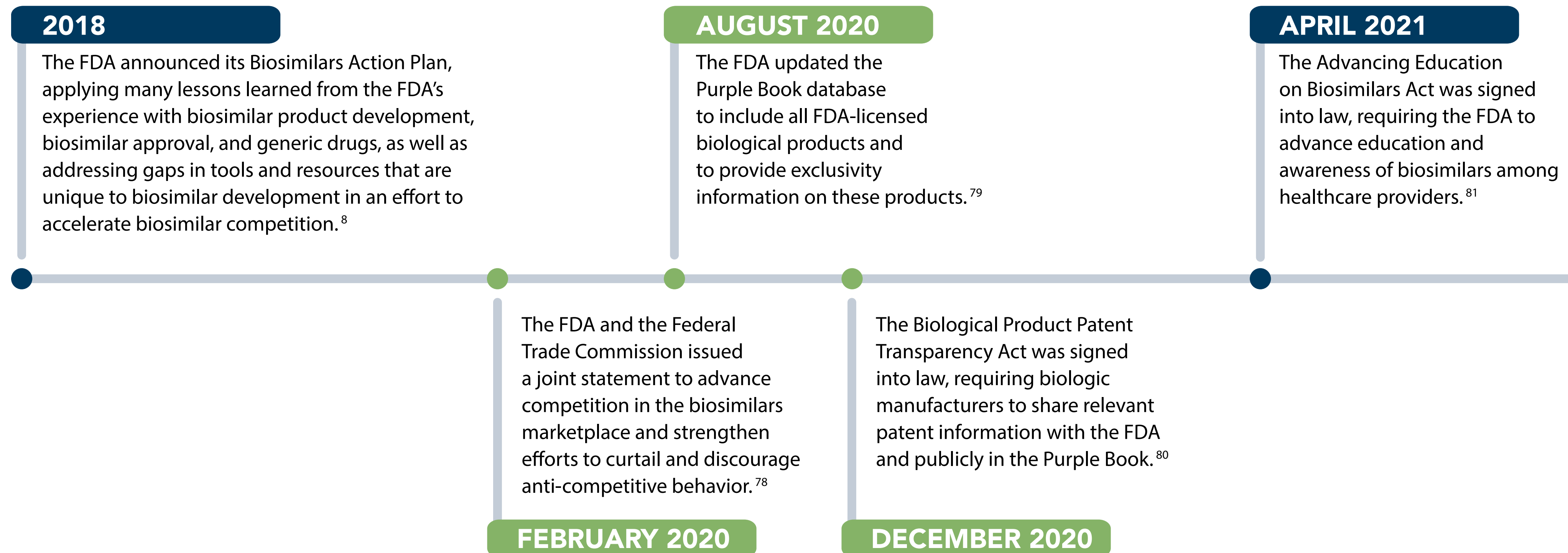
**As we look ahead, biosimilars may continue to offer more affordable biologic treatment options, drive cost savings through increased competition between biosimilars and reference biologics, and promote a more resilient healthcare marketplace. Policy and regulatory actions continue to impact the innovation and adoption of biosimilars and will continue to do so over the next few years.**

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# FEDERAL ACTIONS IMPACTING THE US BIOSIMILARS MARKETPLACE

Through the BPCIA, enacted in 2010, Congress and the FDA established a rigorous, science-based process for the review and approval of biosimilars.<sup>77</sup> Since then, the FDA has continued to review and optimize this process to ensure that patients and providers can rely on the safety, effectiveness, and quality of every biosimilar brought to market.

As a result of the FDA's many efforts, **30 biosimilar products have been approved by the FDA** to date.<sup>12</sup> Further, biosimilar product development in the US continues to grow with **90 programs enrolled in the FDA's Biosimilar Product Development Program.**<sup>10</sup>



Access the Purple Book [here](#).

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# BIOSIMILAR REIMBURSEMENT POLICIES



Policymakers continue to play an important role in helping to set the reimbursement framework for medicines, including biosimilars.

Medicare Part B currently reimburses for reference products and biosimilars with separate payment codes, and this has bolstered the success of the rapidly growing marketplace and allowed manufacturers to invest in delivery devices, patient services, provider education, and a commitment to reliable supply.<sup>82</sup> Congress has also removed financial considerations from clinical decision making by providing that the add-on payment in Medicare Part B is based on the reference product's ASP regardless of whether the provider prescribes a reference product or biosimilar, which allows manufacturers to compete on a level playing field.<sup>83</sup> Beginning in 2019, Congress also provided that biosimilars would be treated the same as reference biologics for purposes of the Medicare Part D Coverage Gap Discount Program, further leveling the playing field.<sup>84</sup> These are examples of productive policy that promotes competition and supports long-term marketplace sustainability.



**Competition has resulted in cost savings for both reference products and biosimilars, while providing additional treatment options for patients.**



With these policies in place, we estimate the cumulative savings in drug spend for classes with biosimilar competition to have been \$9.8 billion over the past 5 years.<sup>3</sup>



We have seen biosimilars gaining significant share in the majority of therapeutic areas where they have been introduced. For therapeutic areas with biosimilars launched in the last 2 years, the average share was 65%.<sup>5</sup>



The prices of biosimilars are decreasing at a CAGR of 9% to 19%. The prices of most reference products are decreasing at a CAGR of 4% to 17%.<sup>2</sup>

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES



# BIOSIMILAR REIMBURSEMENT POLICIES

Several bills have been introduced that impact biosimilar coverage and reimbursement, including HR 2815, the Bolstering Innovative Options to Save Immediately on Medicines (BIOSIM) Act, which would temporarily increase Medicare Part B reimbursement (ASP + 8%) to providers for biosimilars (this policy was included as an amendment to HR 3 in the previous Congress).<sup>85</sup> Other incentive bills include policies that would establish a Medicare “shared savings” demonstration (\$ 1427), reduce cost-sharing for patients to \$0 when they use a biosimilar, and add a new set of measures to the 5-star rating system under the Medicare Advantage program to encourage increased access to biosimilars.<sup>86</sup>

**At the time of publication, none of the abovementioned bills have advanced to impact the reimbursement rate.**

# EDUCATION POLICIES

Separately, policies focused on educating healthcare providers, patients, payers, employers, and the organizations that represent them about biosimilars will be a key part to supporting biosimilar acceptance and use. For example, the bipartisan Advancing Education on Biosimilars Act, signed into law in April 2021, will require the FDA to provide educational materials and programs to patients and providers that demonstrate the safety and effectiveness of approved biosimilars, enhancing confidence in these medicines, with the potential to support uptake and drive healthcare savings.<sup>81</sup>



[Click here](#) for more details regarding the bipartisan Advancing Education on Biosimilars Act of 2021.

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- **POLICY UPDATE**
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# THE 4 KEY ELEMENTS TO A SUCCESSFUL MARKETPLACE WITH BIOSIMILARS

In order to continue to realize the promise of biosimilars – including meaningful cost savings and strengthened healthcare system resilience – over the long term, Amgen believes that the following elements are critical:



## Implementing scientifically appropriate regulatory standards to demonstrate biosimilarity and interchangeability, and to facilitate product identification.

This supports confidence among prescribers and patients. Current standards outlined in FDA guidance for demonstrating biosimilarity and interchangeability are scientifically appropriate and will serve to promote patient safety and build physician confidence when biosimilars are substituted at the pharmacy level.



## Maintaining an environment that encourages head-to-head competition between biosimilars and their reference products on a level playing field and supports long-term resiliency of the marketplace with biosimilars.

This means that in addition to cost savings, manufacturers can compete with important product attributes such as delivery devices, patient support services, provider education, and commitment to reliable supply.



## Providing scientifically accurate educational outreach that helps give all stakeholders confidence and helps support biosimilar acceptance and use.

Help physicians and other healthcare professionals understand the scientific data needed to attain regulatory approval for biosimilars, as well as help build trust that an approved biosimilar will be as safe and effective as its reference product. This allows prescribers to make confident treatment decisions.



## Ensuring a foundation of strong intellectual property protections.

Intellectual property is essential to promoting research and development that delivers cutting-edge medicines and addresses unmet medical needs. A strong intellectual property environment also promotes competition among reference products, biosimilars, and generics.

● INTRODUCTION AND REPORT OVERVIEW

● CURRENT STATE OF THE MARKETPLACE

● FUTURE STATE OF THE MARKETPLACE

● TRENDS

● STAKEHOLDER CONSIDERATIONS

● REIMBURSEMENT

● POLICY UPDATE

● UNDERSTANDING BIOSIMILARS

● REFERENCES



# THE BOTTOM LINE

US policymakers can best nurture a long-term, sustainable marketplace with biosimilars by maintaining effective policies that allow head-to-head competition among reference products and between biosimilars.

If the right balance is struck, biosimilar competition will continue to produce meaningful savings that will endure well into the future. This will allow for a resilient system that supports both biosimilars and new reference products – providing patients, physicians, and payers with a range of treatment options and a degree of flexibility of choice. By continuing to advance science-based policies that support competition and enhance confidence from patients, physicians, and other stakeholders, the US can help promote the robust and resilient healthcare system needed for the long term.

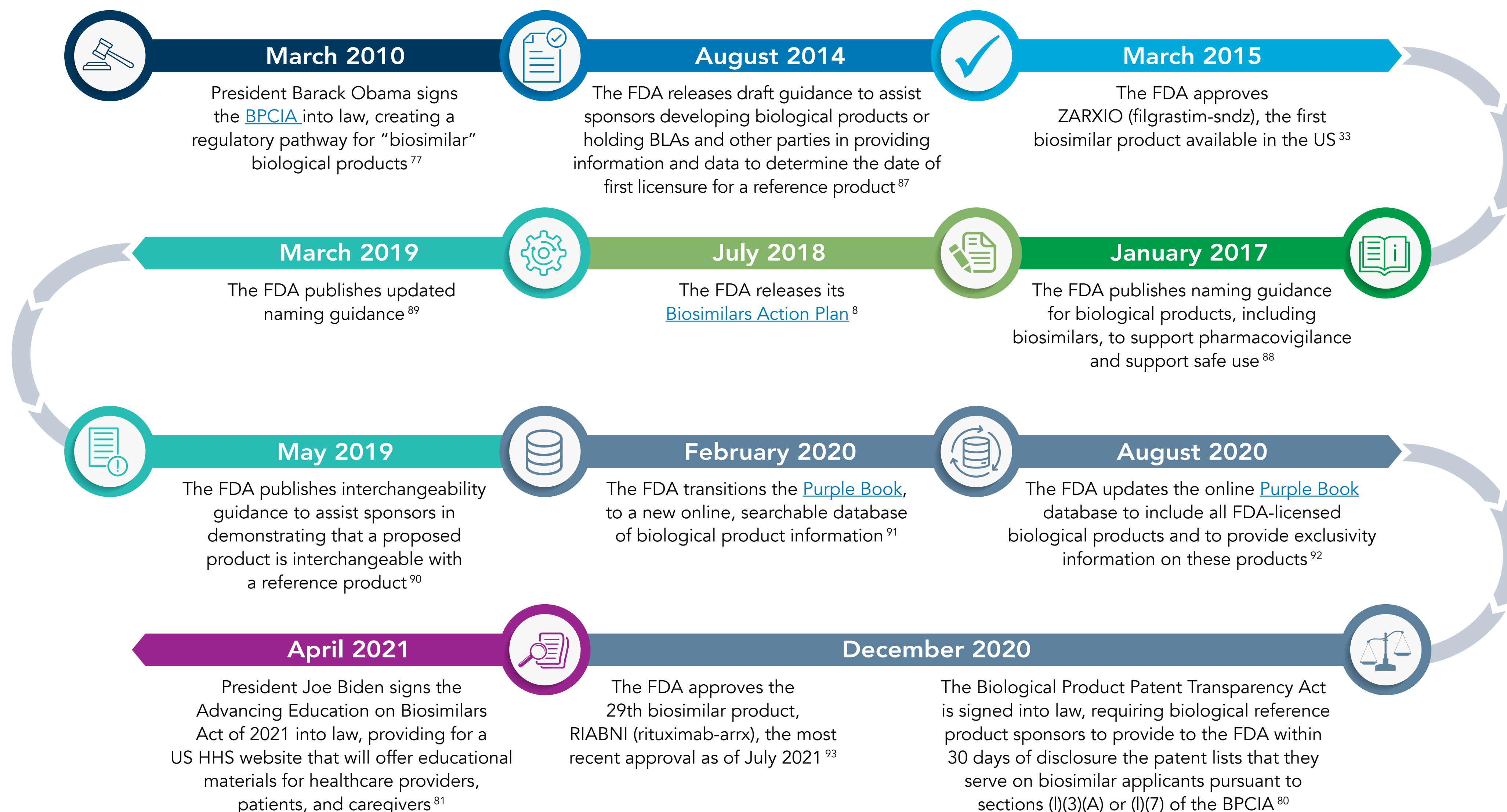


- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES



# A GLANCE AT THE PAST DECADE

## Biosimilar milestones



- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# UNDERSTANDING BIOSIMILARS

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

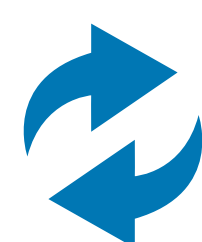
# DEFINING BIOSIMILARS

A biosimilar is a biologic that is highly similar to, and has no clinically meaningful differences from, another biologic that's already approved by the FDA (known as the originator biologic or reference product).<sup>94</sup>

For additional information regarding the fundamental differences between biologics (including biosimilars) and small-molecule drugs (including branded drugs and generics), please refer to Amgen's BioEngage Inside Biosimilars website:



[What Are Biosimilars](#)



[Biosimilars vs Reference Biologics](#)



[Biologics vs Small-Molecule Drugs](#)

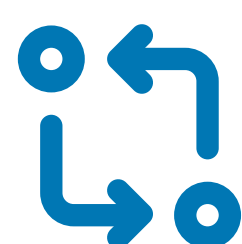
## FDA APPROVAL PATHWAY

The BPCIA, signed into law as part of the ACA in 2010, established the abbreviated approval pathway for biosimilars in the US.<sup>95</sup>

Because biologics contain active substances derived from living cells or organisms, the development of a biosimilar is much more complex than the process for developing a small-molecule generic drug. A biosimilar requires the creation of a new manufacturing process and a custom cell line, since the reference product's manufacturing process is proprietary and not publicly available.<sup>40</sup>

Due to the complex nature and production methods of biologics, relatively minor changes in manufacturing processes may significantly affect product quality, safety, and efficacy.<sup>96</sup>

Based on the provisions in the BPCIA, the FDA recommends a step-by-step biosimilar development approach. At each step in development, an applicant should do the following<sup>97</sup>:



Identify any differences between the reference and biosimilar products



Determine what residual uncertainty about biosimilarity remains based on the potential impact of the observed difference



Design subsequent studies to address the remaining residual uncertainty

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES



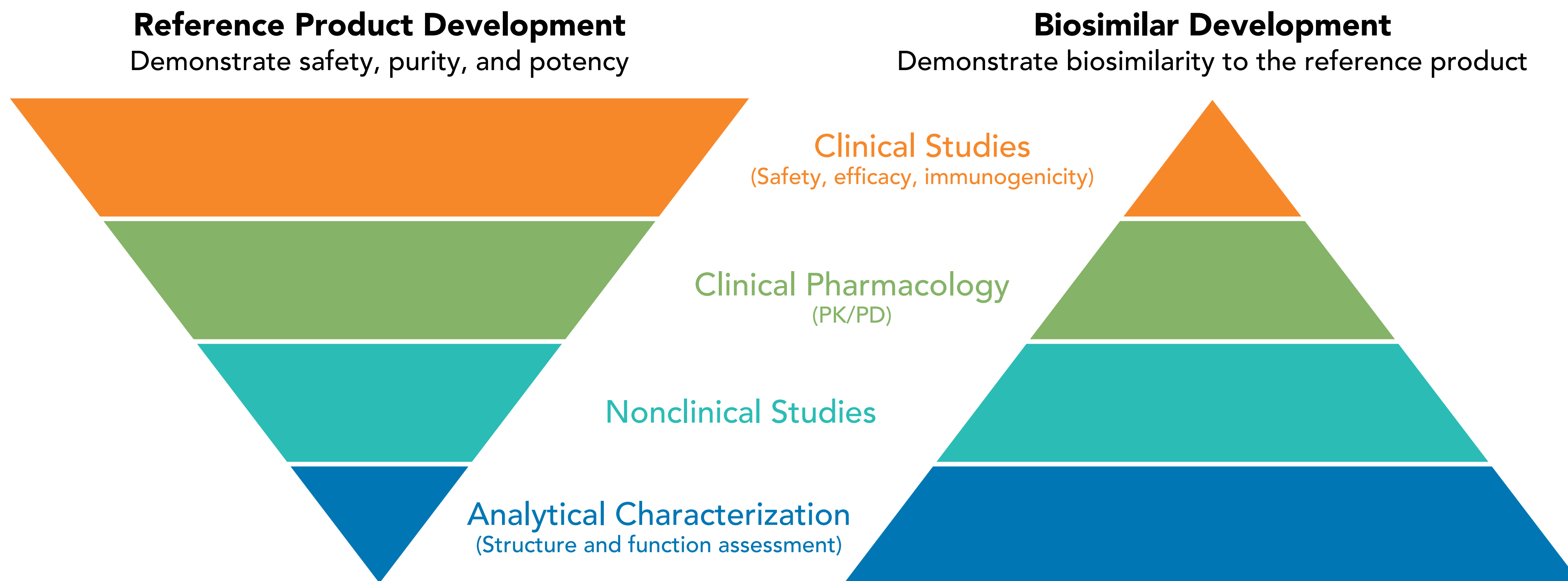
# FDA APPROVAL PATHWAY



As shown in **Figure 39**, while a biosimilar may require more analytical characterization and functional assessments than reference products, it may need fewer clinical trials and clinical pharmacology studies than its reference product to obtain FDA approval.<sup>97</sup> Due to the ability to rely on the FDA's previous finding of safety and effectiveness for the reference product, a biosimilar may have a shorter and less costly development program.

**The BPCIA's abbreviated licensure pathway allows for reliance on the FDA's previous findings of safety and effectiveness for the reference product, promoting a potentially shorter and less costly development program for biosimilars.**

**Figure 39.** Reference Product Development vs Biosimilar Development<sup>97</sup>



- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# FDA APPROVAL PATHWAY



When administered to patients, all biologics – including biosimilars – have the potential to induce an unwanted immune response (ie, to stimulate the formation of antidrug antibodies). The impact of immune responses, or “immunogenicity,” can range from no apparent effect to changes in pharmacokinetics, loss of effect, and serious adverse events.<sup>98</sup>

Understanding a biologic’s immunogenicity profile is key to establishing the safety profile of all biologics. A head-to-head assessment comparing immunogenicity of the biosimilar with that of the reference product is, therefore, of critical importance. It is considered a key component of a biosimilar’s clinical development program.<sup>98</sup>

**The goal of a biosimilar development program is not to independently establish the safety and efficacy of the biosimilar product, but to demonstrate that the proposed biologic product is biosimilar to the reference product. No single study is considered “pivotal” to a biosimilar application; rather, the totality of data and information submitted to the FDA support the demonstration of biosimilarity.**

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# EXTRAPOLATION, INTERCHANGEABILITY, SWITCHING, AND SUBSTITUTION

While reference products with multiple indications require clinical studies to establish safety and efficacy for each indication, biosimilars are not required to be evaluated clinically in every indication held by the reference product for which approval is sought. Instead, a manufacturer of a biosimilar can “extrapolate” data and information supporting biosimilarity in one condition of use to other conditions of use for which the reference product is licensed.<sup>99</sup>

In general, it is likely that a biosimilar will be approved for all of the reference product's approved indications. However, a biosimilar may be approved for fewer indications than the reference product.

A “biosimilarity” determination by the FDA is a necessary but not sufficient finding to support substitutions at the pharmacy. The FDA designates a biosimilar as “interchangeable” if, in addition to demonstrating biosimilarity, the manufacturer demonstrates<sup>99</sup>:



The product can be expected to produce the same clinical result as the reference product in any given patient



For a product that is administered more than once to an individual, the risk in terms of safety or diminished efficacy of alternating or switching between use of the product and the reference product is not greater than the risk of using the reference product without such alternation or switch

**To support a demonstration of interchangeability, FDA guidance indicates that it is generally expected for a manufacturer to conduct 1 or more “switching studies” that will assess the safety or efficacy of alternating between the reference biologic drug product and the biosimilar.<sup>90</sup>**



For more details regarding indication extrapolation, refer to Amgen’s short video [“The Scientific Justification for Extrapolation.”](#)

An interchangeable biosimilar product may be substituted for the reference product by a pharmacist without the involvement of the prescriber (pursuant to state pharmacy laws). All 50 states plus DC and Puerto Rico have passed legislation to allow a pharmacist to substitute a biosimilar for its reference product at the pharmacy as of July 2021.<sup>29</sup>

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# PHARMACOVIGILANCE AND NAMING



Pharmacovigilance, the monitoring and tracking of drug safety over time, is important to detect any emerging safety signals of any biologic, including biosimilars.<sup>100</sup> To help facilitate pharmacovigilance, the FDA released final guidance on the nonproprietary naming of biological products (including biosimilars) in January 2017.<sup>88</sup>

Generic drugs and their brand drugs share the same nonproprietary name because they are chemically identical. However, reference biologics and biosimilars are highly similar but not chemically identical. Distinguishable nonproprietary names facilitate pharmacovigilance and help avoid inappropriate substitution at the pharmacy level.<sup>88</sup>

Under the guidance, each new originator biologic, related biologic, and biosimilar will be assigned a nonproprietary name consisting of a core name and a hyphenated distinguishing suffix of 4 lowercase letters.<sup>88</sup>

The example in **Table 5** shows hypothetical nonproprietary names of a reference product and its biosimilar:

**Table 5.** Comparison of Nonproprietary Names of Reference Products and Biosimilars<sup>88</sup>

	Core name	Distinguishing suffix
Reference product	Same core name	-agdb
Biosimilar	Same core name	-eyfp



For more information regarding the purpose of the FDA's policy regarding naming, refer to Amgen's "Prescribing Biosimilars/Naming" article on the [BioEngage website](#).

The benefits of the naming convention should bolster patient and physician confidence and encourage manufacturer accountability by providing additional ways to help track prescribed products appropriately.<sup>88</sup>

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# REFERENCES

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- **REFERENCES**



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- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# REFERENCES



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- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# REFERENCES



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- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# REFERENCES



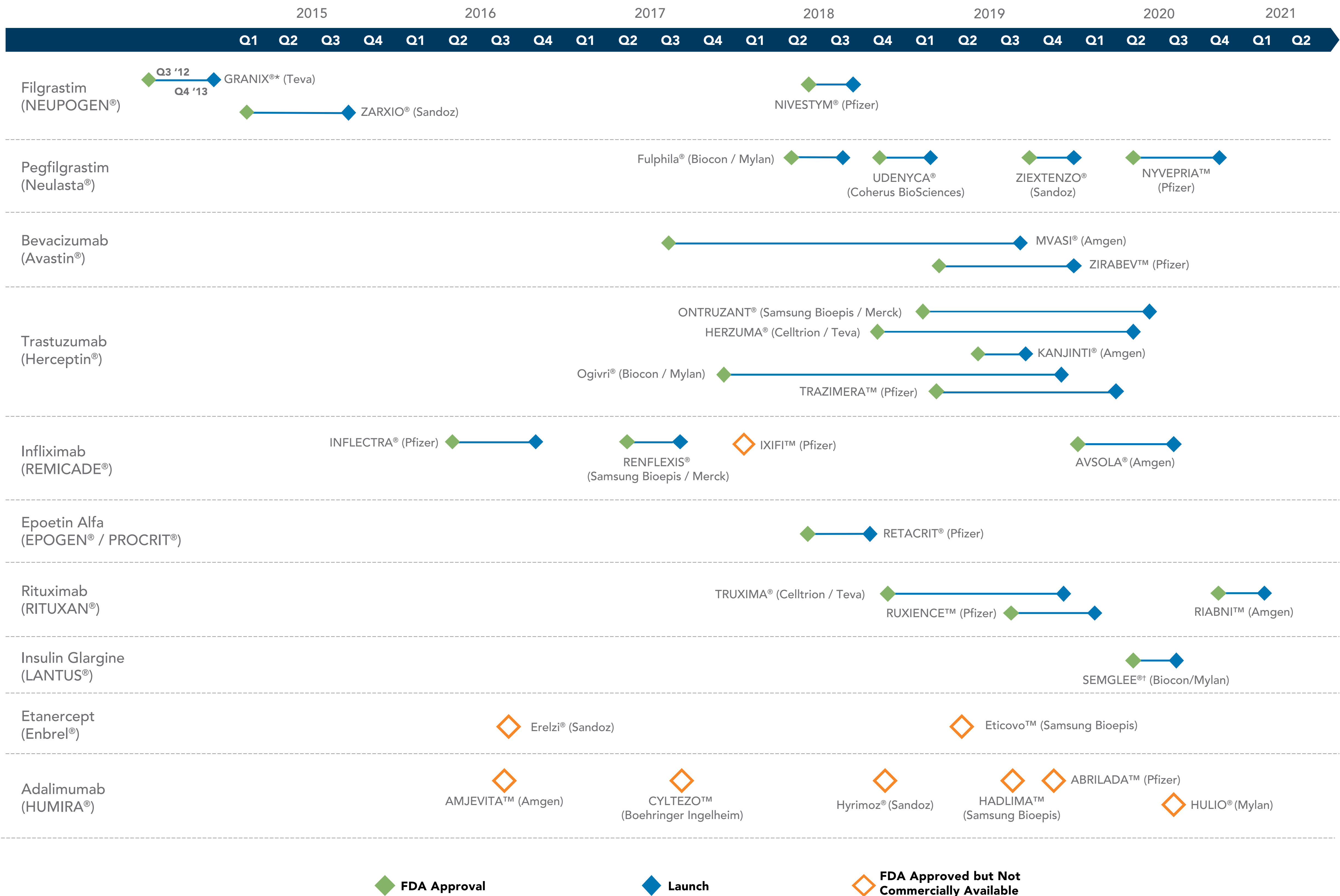
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- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

# APPENDIX

- INTRODUCTION AND REPORT OVERVIEW
- CURRENT STATE OF THE MARKETPLACE
- FUTURE STATE OF THE MARKETPLACE
- TRENDS
- STAKEHOLDER CONSIDERATIONS
- REIMBURSEMENT
- POLICY UPDATE
- UNDERSTANDING BIOSIMILARS
- REFERENCES

**Figure 3. Approved and Launched Biosimilars (including GRANIX\*) in the US<sup>1</sup>**

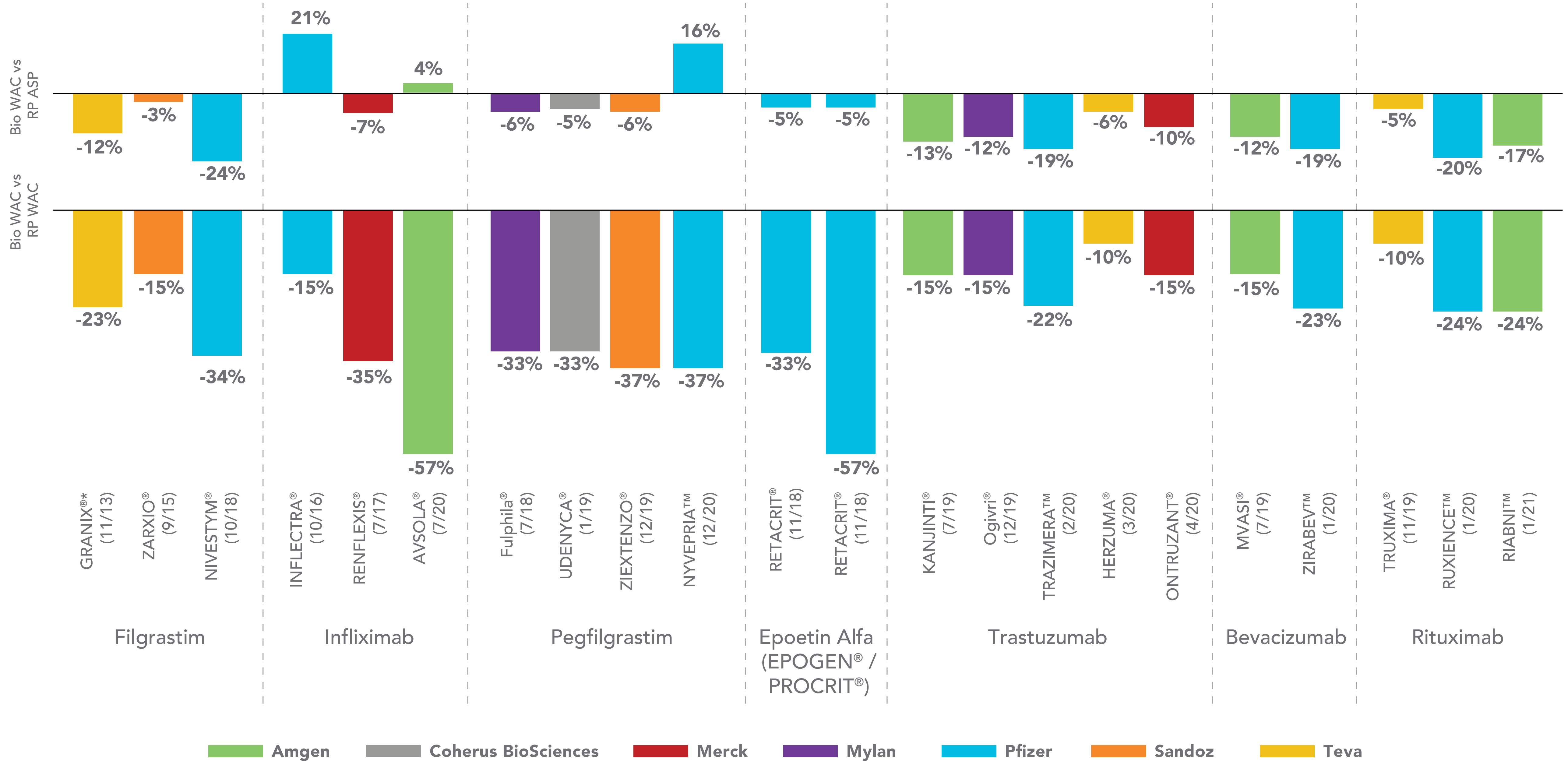


Please [click here](#) for Boxed Warning information for AVSOLA, EPOGEN, Enbrel, KANJINTI, and RIABNI.

Key: BLA – Biologics License Application; FDA – Food and Drug Administration; US – United States.  
 \*GRANIX is not a biosimilar. It was approved under a stand-alone BLA, which was submitted to the FDA before the enactment of the biosimilar approval pathway.  
 †SEMGLEE was approved by the FDA in June 2020 with a stand-alone BLA. The FDA subsequently approved SEMGLEE as an interchangeable biosimilar in July 2021.<sup>11</sup>

**Figure 4. Price at Launch vs Reference Product<sup>2</sup>**

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Biosimilar WAC vs Reference Product ASP:

**Almost all biosimilars have launched at a WAC 3% to 24% below the reference product ASP.**

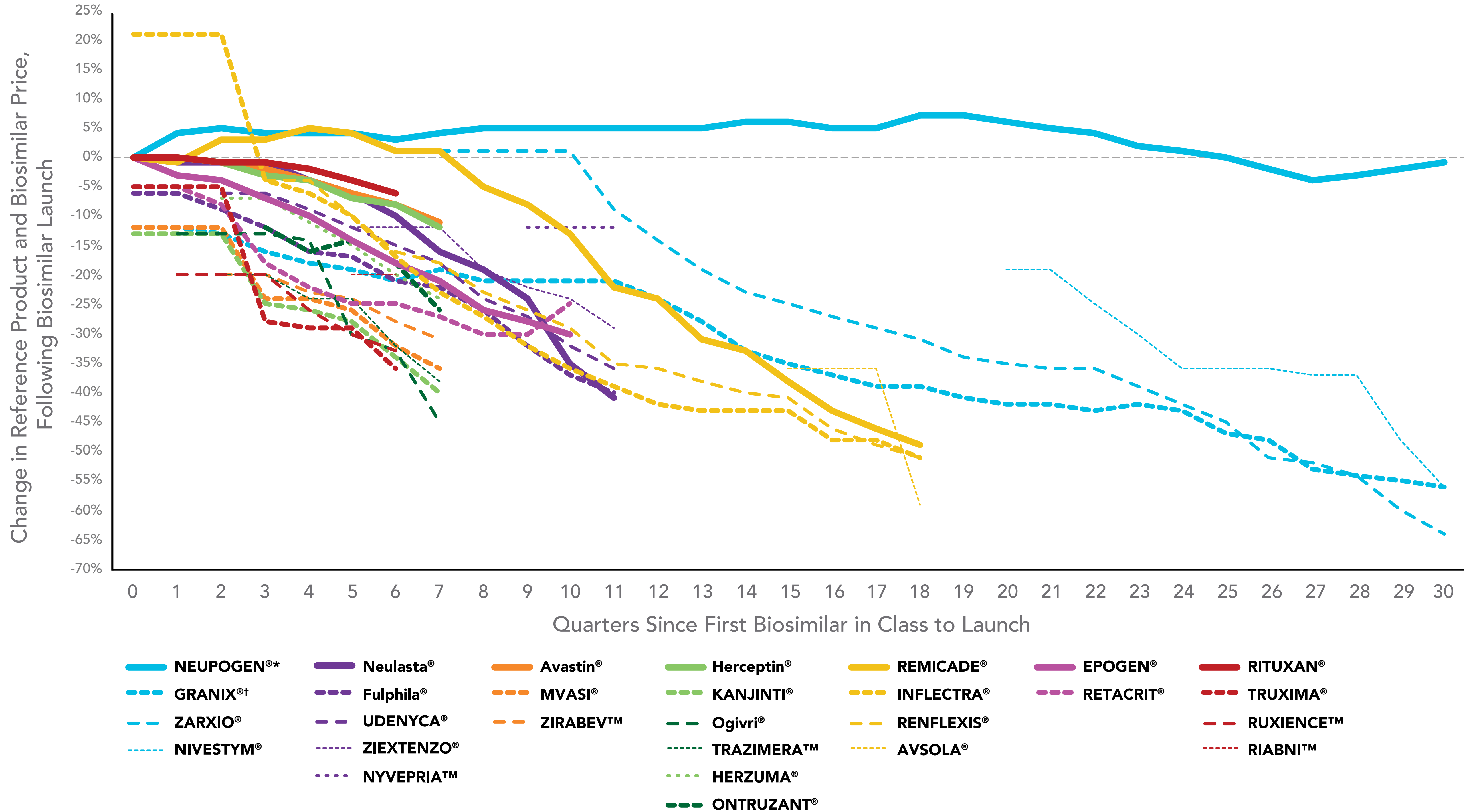
Biosimilar WAC vs Reference Product WAC:

**Biosimilars launch at a WAC that is generally 15% to 37% lower than the reference product.**

Please [click here](#) for Boxed Warning information for AVSOLA, EPOGEN, Enbrel, KANJINTI, and RIABNI.

Key: ASP – average sales price; Bio – biosimilar; FDA – Food and Drug Administration; RP – reference product; WAC – wholesale acquisition cost.  
 \*GRANIX is not a biosimilar. It was approved under a stand-alone Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.  
 Source: AnalySource.

**Figure 5. Downward Trend in ASP for Biosimilars and Reference Products Over Time<sup>2</sup>**



**The prices of biosimilars are decreasing at a CAGR of 9% to 19%.**

**The prices of most reference products\* are decreasing at a CAGR of 4% to 17%.**

Please [click here](#) for Boxed Warning information for AVSOLA, EPOGEN, Enbrel, KANJINTI, and RIABNI.

Key: ASP – average sales price; CAGR – compound annual growth rate; FDA – Food and Drug Administration.

\*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.

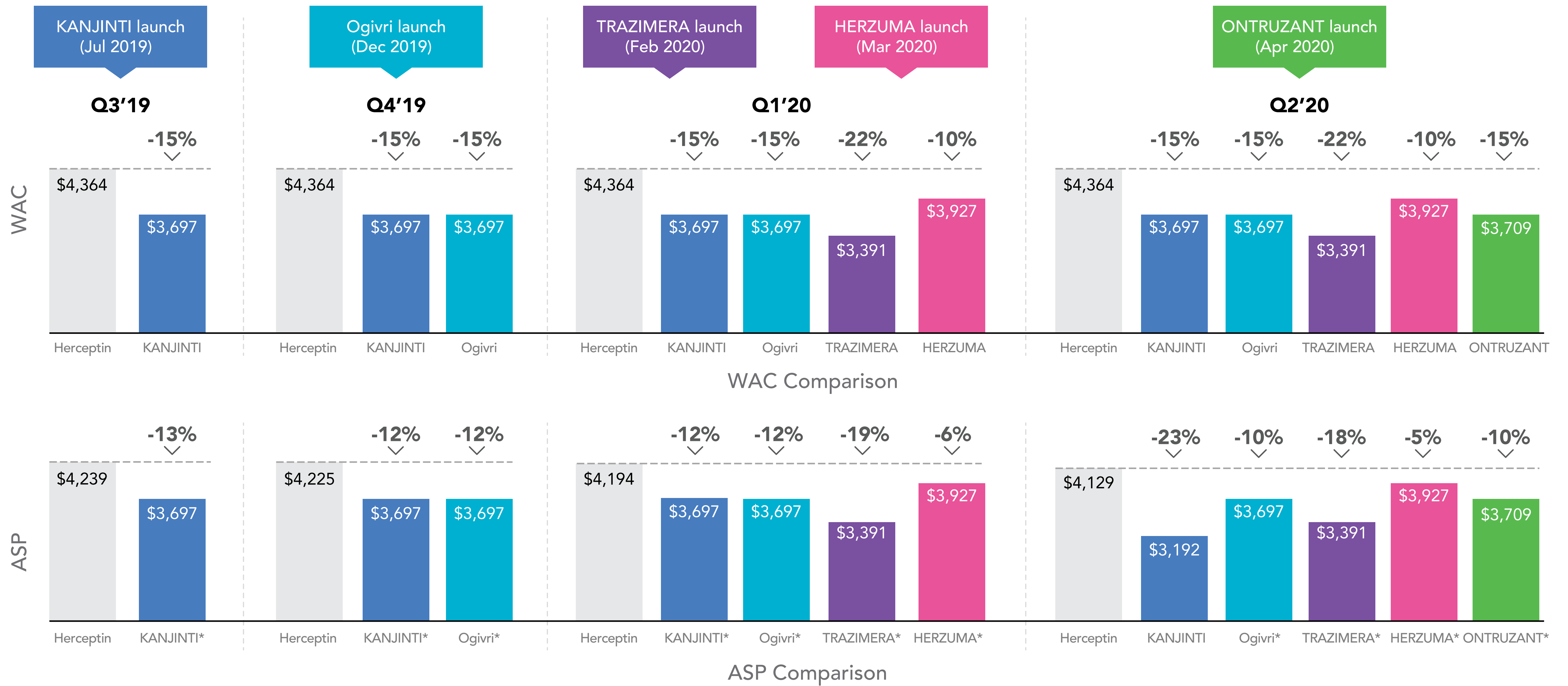
†GRANIX is not a biosimilar. It was approved under a stand-alone Biologics License Application, which was submitted to the FDA before the enactment of the biosimilar approval pathway.

Source: AnalySource.



**Figure 11. WAC and ASP of Trastuzumab Biosimilars Relative to Reference Product at Launch<sup>2</sup>**

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Please [click here](#) for Boxed Warning information for KANJINTI.  
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Key: ASP – average sales price; WAC – wholesale acquisition cost.  
\*ASP was not available for these products at the time of comparison. WAC is used to compare with reference product ASP.  
Source: AnalySource.

