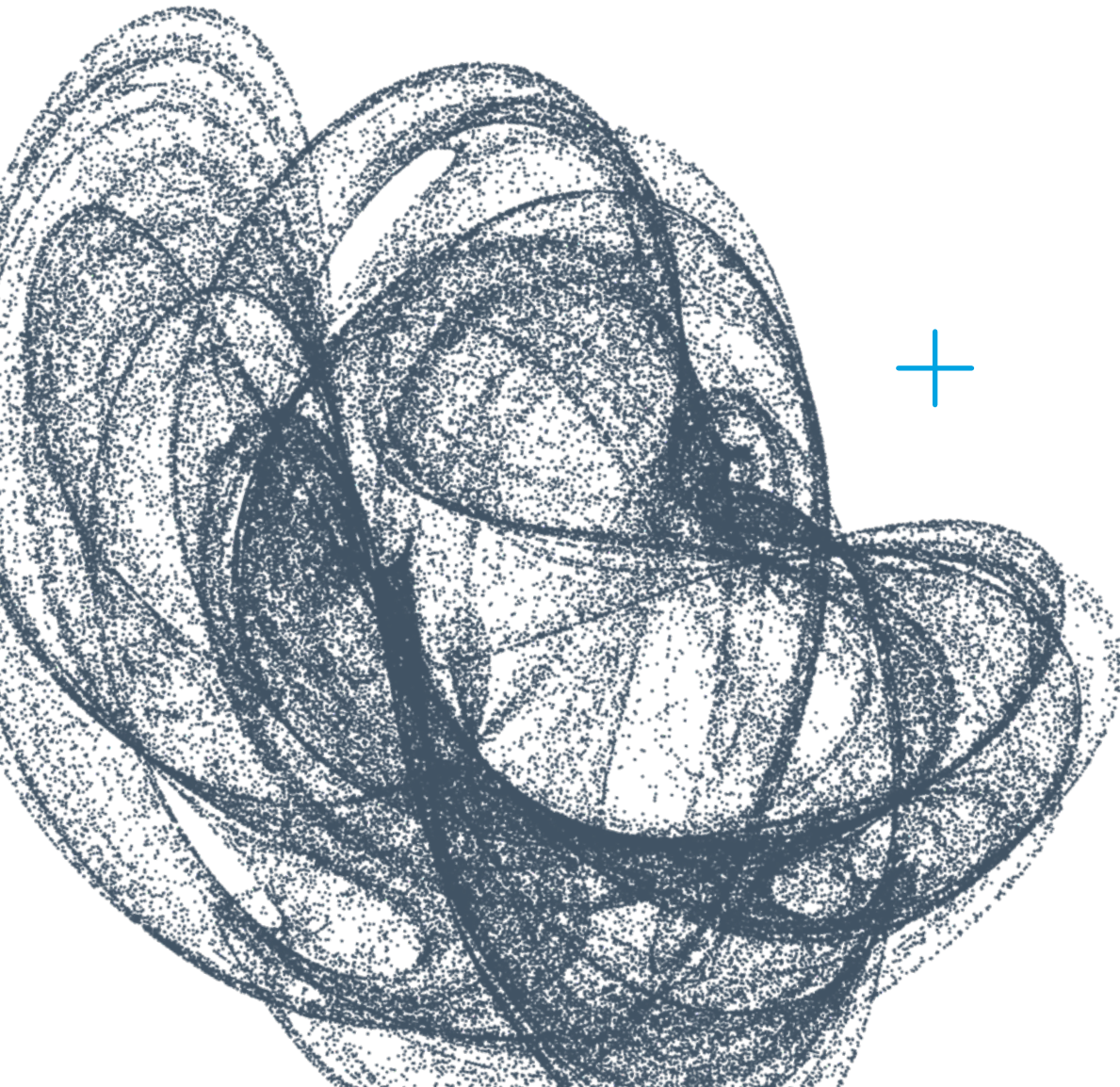


Biosimilars in the United States 2020–2024

COMPETITION, SAVINGS, AND SUSTAINABILITY



OCTOBER
2020

Introduction

The regulatory pathway to approve ‘biosimilar’ competitors was signed into U.S. law in 2010, but savings have been slow to materialize until recently. Early biosimilars have been few in number and generated limited savings compared to expectations. Slower uptake and muted savings raise fundamental questions around defining the success of biosimilars for all stakeholders, and particularly patients. By contrast, recent events suggest an inflection has occurred and events expected in the next few years potentially offer to bring further significant shifts.

In this report the current state of the biologics market in the United States is assessed, with the market segmented into the part currently facing biosimilar competition, parts that are not, and those molecules that may never face biosimilar competitors. The current segment facing biosimilar competition is more substantial than some might expect and is key to understanding the potential systemic savings that may be generated by biosimilars in the future.

Experience to date also informs the scenarios likely to play out based on the market incentives and the actions of participating companies over the coming years. Some commonly held assumptions about patient and provider acceptance and comfort with biosimilars appear to be more conservative than data demonstrate, providing valuable insight into the outlook for biosimilars and medicine spending overall.

To afford the medicines patients need, while driving continued innovation to address unmet needs, older effective treatments must become cheaper. In this context the importance of biosimilars to not only save money but also generate headroom for future breakthroughs cannot be overstated.

This study was produced independently by the IQVIA Institute for Human Data Science as a public service, without industry or government funding. The contributions to this report of Aurelio Arias, Allen Campbell, Deanna Nass, Max Newton, Alana Simoneellis, Durgesh Soni, Per Troein, Terri Wallace, and dozens of others at IQVIA are gratefully acknowledged.

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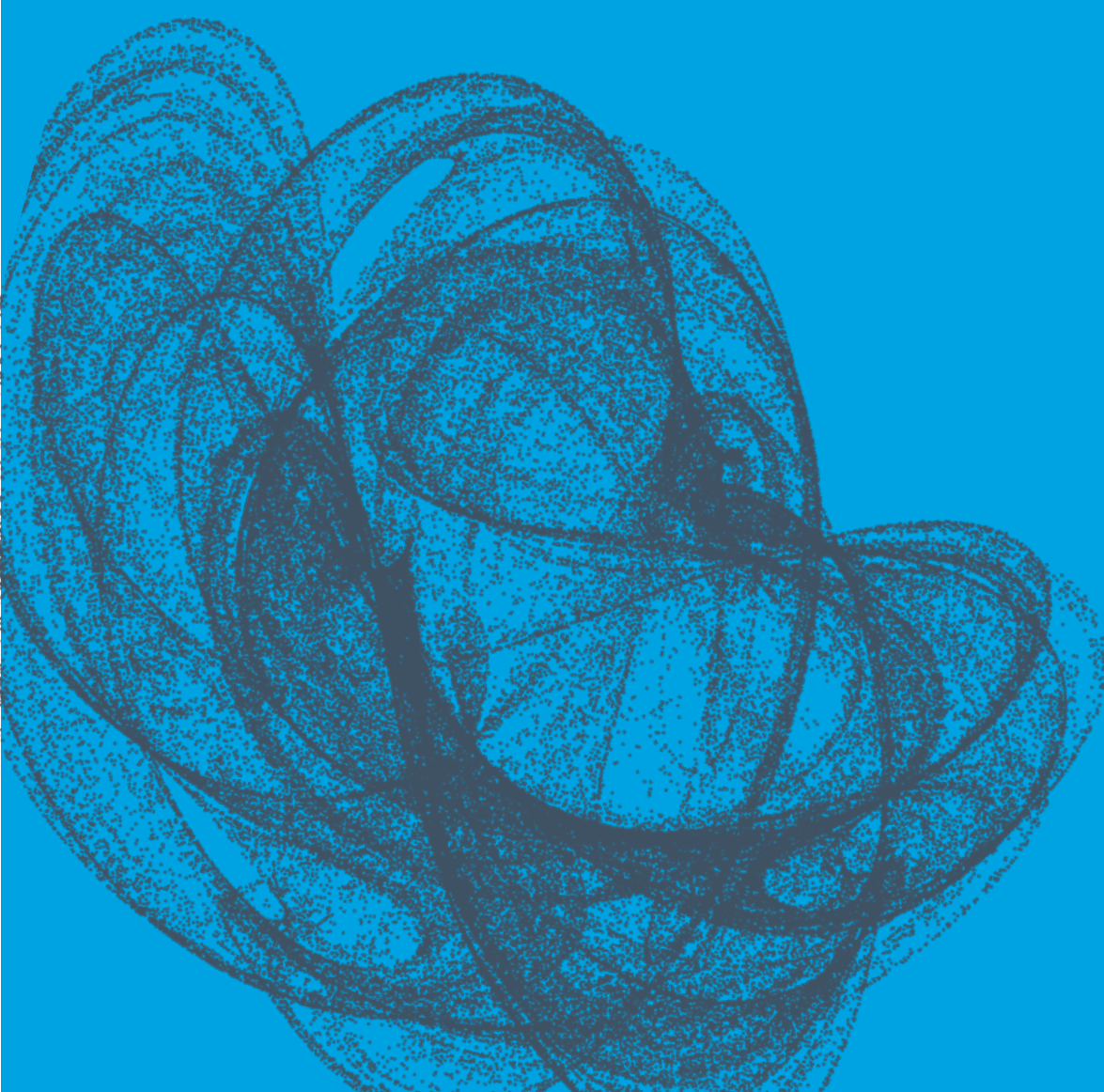
Executive Director

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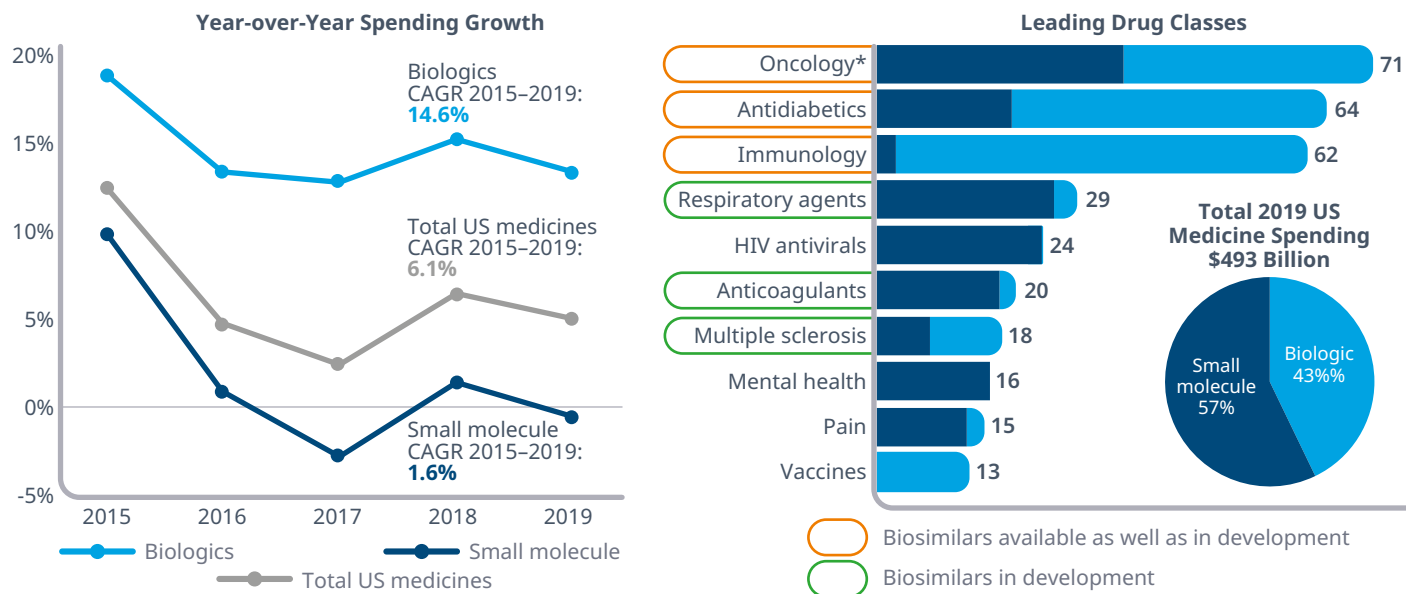


Overview

- Biologics represent 43% of invoice-level medicine spending in the United States, reaching \$211 billion in 2019, and growing at a 14.6% compound annual growth rate (CAGR) over the past five years. This compares to a 6.1% CAGR for the total market comprising small molecules, biologics, and biosimilar competitors.
- While molecules representing 51% of current biologic spending are already facing biosimilar competition, or will face it within the next ten years according to the current biosimilar pipeline, the remaining 49% of current spending is from molecules that may not be near-term biosimilar targets. This may be because they are only recently launched and are still protected for the next decade, or may have too little revenue to attract competitors.
- Development and approvals of biosimilars have been accelerating, with 33 approvals across 13 molecules to date, though biosimilars for only 11 molecules have launched. One-hundred and eight additional biosimilars are in development across 22 other molecules.
- Large pharma companies, often with existing innovative biologic portfolios, have dominated the marketing of biosimilars to date, while smaller companies are developing biosimilars but are likely to license products to a larger company for marketing.
- The 22 launched biosimilars in aggregate have 20% volume share of the accessible market, which represents about 16% of biologic sales. Approved but not yet launched products represent another 17% of the biologics market, bringing the total to 36% of current biologic spending.
- Recent biosimilar launches of bevacizumab, trastuzumab, and rituximab are set to reach nearly 60% volume share by the end of their second year on the market, significantly higher and faster than prior biosimilars.
- Provider adoption of biosimilars has been highly heterogenous. Bevacizumab is the molecule with the fastest biosimilar uptake to date, reaching 42% of volume by June 2020, a year after the first biosimilar launch. Among leading providers, bevacizumab biosimilar use ranges from 0–100%, with some providers avoiding having to manage switching of non-interchangeable products by treating with only a biosimilar or the originator, while the majority of providers are using both, though the extent of switching is not yet clear.
- The introduction of biosimilars in some cases has generated 2–4% incremental demand for the molecule, bringing new lower-cost options to more patients.
- Price declines for biosimilars range significantly but appear to reflect prior assumptions of roughly 30% discounts, though higher discounts have occurred and are possible in the future.
- Biosimilars could reach \$80 billion in aggregate sales over the next five years, including \$16–36 billion in 2024.
- Savings enabled by the presence of biosimilars are modeled to exceed \$100 billion in aggregate over the next five years, though volume and price dynamics remain volatile and significant uncertainty remains.

The U.S. biologics market continues to grow faster than non-biologics on an invoice-basis, and now comprises 43% of spending

Exhibit 1: Total U.S. Invoice Spending Growth by Type and Leading Therapy Areas by 2019 Spending, US\$Bn



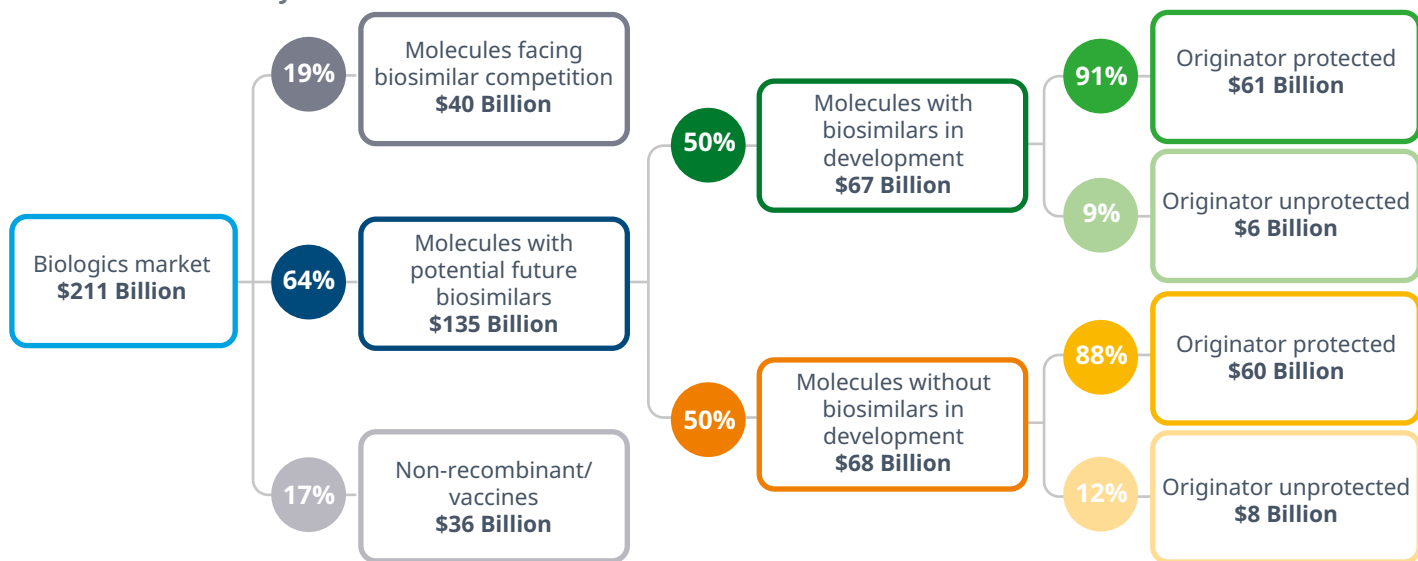
Source: IQVIA MIDAS®; IQVIA Institute, Jun 2020

- In 2019, the United States spent \$493 billion on medicines at ex-manufacturer invoice prices, including \$211 billion on biologics, which now comprise 43% of total medicine spending.
- Manufacturer net revenues for medicines, after discounts and rebates are reflected, totaled \$356 billion, of which 48% stem from sales of biologics.
- Even including the effect of biosimilar competition over the past decade, biologics spending increased significantly since 2014, at a compound annual growth rate (CAGR) of 14.6%, outpacing the 1.6% CAGR for small molecules and raising the total market CAGR to 6.1%.
- The three classes with the highest spending — oncology,* antidiabetics, and immunology agents — account for 66% of biologics spending, and their biologics growth is at 21.0%, 13.7%, and 21.2% CAGRs, respectively, in the past five years.
- Respiratory agents and pain medicines have seen substantial growth in biologics, with 31.2% and 36.6% CAGRs since 2014, respectively, due to advances in severe asthma and migraine treatments.
- Several biosimilar launches occurred in the top three spending areas since 2007, including biosimilar colony-stimulating factors, insulins, and immunomodulating agents.
- Additional biosimilars are in development in these classes, as well as in respiratory agents, anticoagulants, and multiple sclerosis products.
- Smaller classes of medicines, such as growth hormones and osteoporosis treatments also have biosimilars available, and biosimilars are in development for anti-neovascularization treatments and immunosuppressants.

Exhibit Notes: *Oncology includes therapeutic agents as well as supportive care.¹ For autoimmune and pain therapy definitions, please see IQVIA Institute Report: *Medicine Spending and Affordability in the United States*.² Invoice prices in this report are ex-manufacturer level, reflecting the prices between manufacturers and their customers (wholesalers or direct purchasers).

Molecules with biosimilars total \$40 billion of invoice spending, while biosimilar development is targeting a further \$67 billion

Exhibit 2: 2019 Biologics Market Segmented by Status of Biosimilar Competition, Biosimilar Development and Market Exclusivity



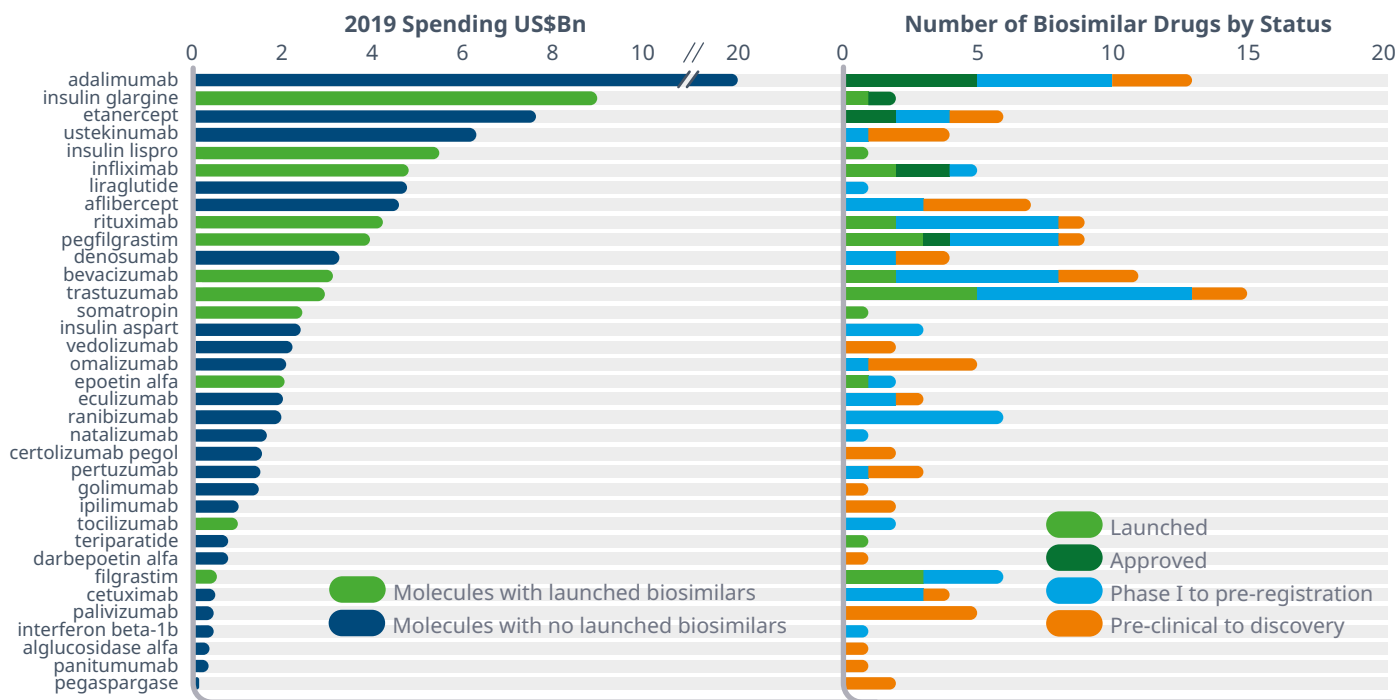
Source: IQVIA MIDAS®; IQVIA Pipeline Intelligence, IQVIA Institute, Jun 2020

- The current biologics market of \$211 billion at ex-manufacturer invoice prices is already facing some biosimilar competition, with \$40 billion, or 19%, of the market currently exposed to biosimilar competition (i.e., exposed originators and their competitor biosimilars), giving patients and payers lower cost options.
- An additional 17% of the market, or \$36 billion, are biologics produced without recombinant technologies, such as purified or gathered biologics, thereby making it impossible to produce a biosimilar, though in some cases, non-recombinant biologics are already facing generic competition as they are naturally occurring substances or vaccines without patent protection.
- The remaining 64%, or \$135 billion, is potentially open to biosimilar competition. The market is nearly evenly split between molecules where biosimilars are currently in development (\$67 billion) and those where they are not (\$68 billion).
- There are 24 molecules with biosimilars approved or in development: 20 where the originator remains protected by exclusivity, and four that are unprotected.
- Protected molecules with biosimilars in development generated \$61 billion in sales, including the blockbusters adalimumab (Humira) and etanercept (Enbrel). Based on current patents, 17 of these molecules are expected to lose exclusivity by 2025, representing \$55 billion in 2019 sales.
- There are 153 molecules without biosimilar development, comprising the remaining \$68 billion of sales. Of these, 125 are currently protected, generating \$60 billion, while the remaining 28 are off-patent and generating \$8 billion.
- Of the protected molecules without biosimilars in development, 29% are expected to go off patent by 2025, representing \$9.7 billion.

Exhibit Notes: Protected is defined as having an expiration date in the future, while unprotected is defined as having an expiration date in the past. Invoice prices in this report are ex-manufacturer level, reflecting the prices between manufacturers and their customers (wholesalers or direct purchasers). Generics for non-recombinant biologics include glatiramer acetate, enoxaparin sodium, and a range of vaccines and blood plasma products.

There are biosimilars launched, approved, or in development for 35 molecules

Exhibit 3: Current Total Molecule Spending and Approved, Launched and Pipeline Biosimilar Products for the Molecule



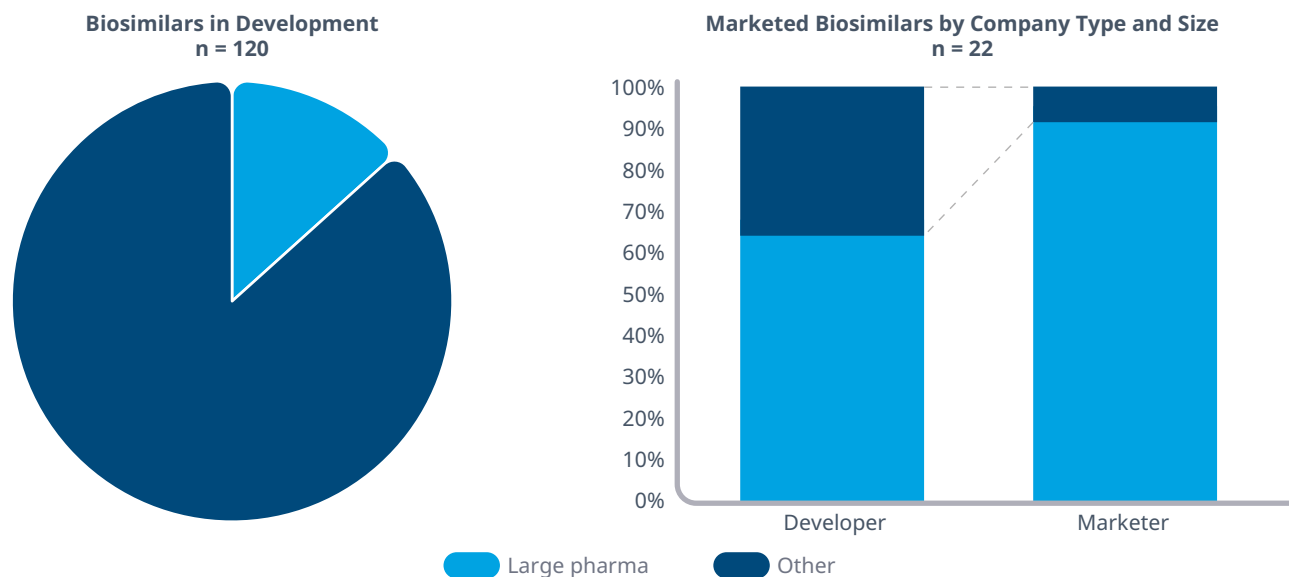
Source: IQVIA Institute, Sep 2020; IQVIA Biosimilar Database, Jun 2020

- To date, there are 22 molecules in development, eleven molecules that already have biosimilar competition, and an additional two that have been approved and are awaiting launch. The ones awaiting launch are biosimilars for adalimumab and etanercept, some of the highest revenue biologics, which are on hold due to patent litigation agreements.
- For other products, such as insulin glargine and insulin lispro, biosimilars have been launched and there are now very few, if any, additional biosimilars in development. This is, in part, due to technical complexities of manufacturing insulin and the extremely deep market discounts that predominate and thus limit potential financial returns.
- Of the 35 molecules with biosimilars under development, 18 have attracted three or more biosimilar competitors, while the remaining molecules have attracted fewer.
- The correlation between the magnitude of molecule sales and the number of biosimilar competitors attracted to the space is not as robust as expected. Rather it appears that the selection of molecules for biosimilar development may be influenced by multiple factors such as technical complexity, intellectual property issues, or expected market size, which could be lower now than was anticipated when biosimilar programs were started.
- There are no biosimilars in development for the 82 molecules with sales below \$100 million, where there is less room for return on investment.
- The lowest-selling molecule to attract biosimilar development is pegaspargase (Oncaspar), a rare disease medicine, with \$183 million net sales in 2019. Rare disease drugs typically have different market dynamics, enabling biosimilar development even in lower sales molecules.³

Exhibit Notes: Sales values reported from IQVIA MIDAS® audited ex-manufacturer invoice sales; For products with known understated revenues, sales values are reported from public sources. Pipeline includes biosimilar medicines with development programs in the United States or other developed markets with regulatory filings in the United States or publicly stated intent to do so.

Development of biosimilars is being driven by smaller companies, while marketing is done mostly by large companies

Exhibit 4: Biosimilars in Development and Marketed in the United States by Company Type and Size



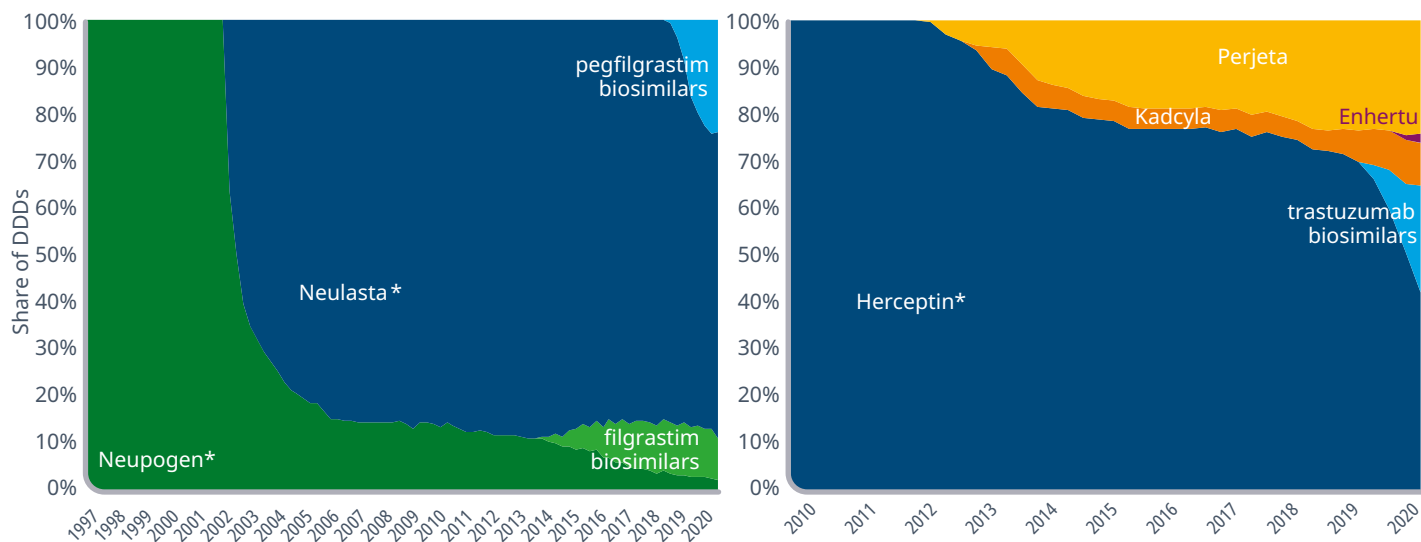
Source: IQVIA Institute, Sep 2020; IQVIA Biosimilars Database, Jul 2020

- Currently, 13% of the biosimilar products in the pipeline are being developed by six large pharma companies; those with more than \$10 billion global sales. The remaining 87% are being developed by 41 smaller companies with varying degrees of biologic or biosimilar development experience.
- Large pharma companies, including large generic companies Teva and Mylan, are typically developing biosimilars to diversify their originator biologics business, and in some cases offer a portfolio of both originator and biosimilar biologics in the same therapy area.
- Of biosimilar products marketed in the United States, 14 were developed and launched by seven large pharma companies: Sandoz developed and launched three, while Pfizer developed three and also acquired and launched two more after their Hospira acquisition in 2015.
- Several of the smaller companies are niche biosimilar makers that focus on biosimilar development but, to date, have licensed their products to other companies for commercialization. These include companies such as Celltrion and Samsung Bioepis.
- There are six biosimilar products that were developed by companies that focus specifically on biosimilar-development yet were marketed by large pharmas. The most prolific developer is Celltrion, which developed three biosimilars. Two of the products were commercialized by Teva, and the third by Pfizer.
- Only one product has been developed and launched by a smaller company, Coherus Biosciences, highlighting the likelihood that the complexities and costs of marketing biosimilars are likely filtering out smaller competitors.

Exhibit Notes: Large pharma are those with >\$10 billion global sales and includes companies regardless of strategy, and large global generic companies Teva and Mylan are categorized as large. Other refers to all other companies with a biosimilar in development, regardless of biologic or biosimilar experience.

Patient access to successive generations of originator products has narrowed the biosimilar-accessible market

Exhibit 5: Quarterly Share of Defined Daily Doses (DDDs) by Originators, Second Generation Originators and Biosimilars in Selected Markets



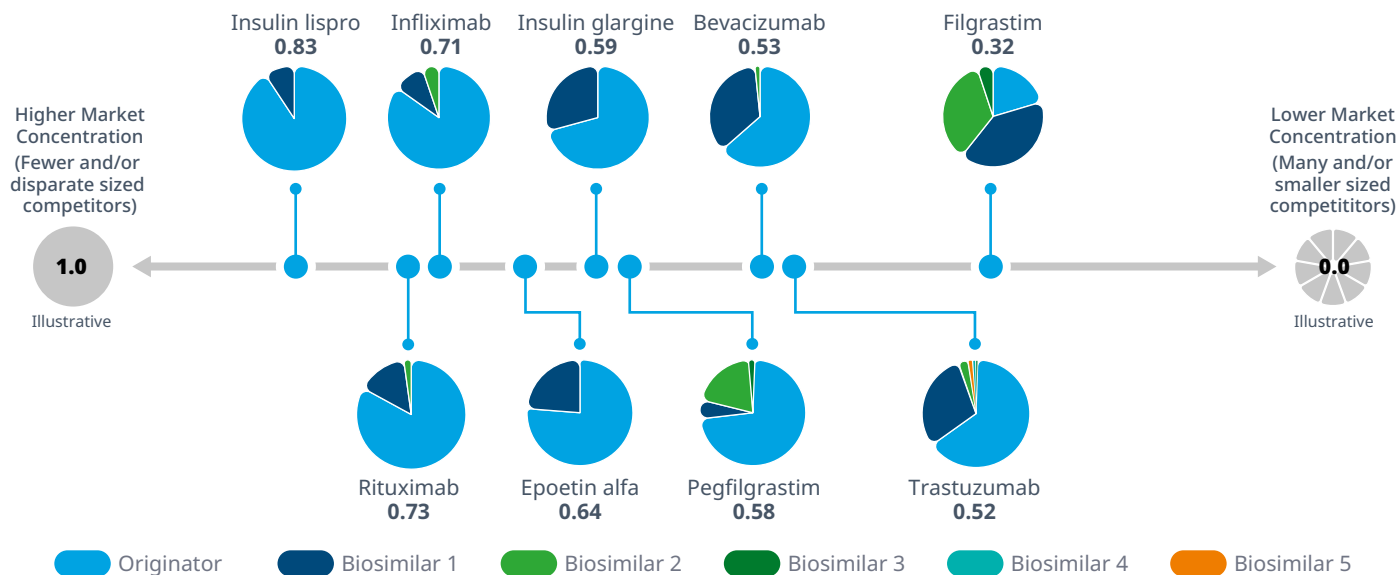
Source: IQVIA National Sales Perspectives; IQVIA Institute, Jun 2020

- Taking a longer-term view of the volume of two markets as examples, newer-generation medicines can supersede the first originator and change the size of the market ultimately accessible to biosimilars.
- As biosimilar makers identify and prioritize molecules to develop, the size of the accessible market is a critical factor in determining potential financial returns and their strategy. The accessible market may fluctuate due to either shifts in volume, driven by lower costs that increase access, or by increased adoption of newer originator products.
- In the colony-stimulating factor market, the shift from filgrastim to pegylated filgrastim (pegfilgrastim) has been underway for many years, yet slightly reversed with the launch of biosimilars as volume shifted back to filgrastim.
- The group of products in breast cancer, while not a full view of all breast cancer treatments, illustrates the days of therapy accessible to trastuzumab biosimilars has been reduced by almost 30%, as newer generation products were increasingly adopted prior to the introduction of biosimilars in July 2019.
- Additionally, over this extended period, biosimilar filgrastim captured 80% of molecule volume in six years, much higher than typical biosimilar uptake assumptions over the long term. This demonstrates that even with a slow early uptake, biosimilars can hold a significant portion of the market.

Exhibit Notes: * Originator product where biosimilars are available for the same molecule: filgrastim (Neupogen), pegfilgrastim (Neulasta), trastuzumab (Herceptin). Trastuzumab emtasine (Kadcyla) is an antibody drug conjugate. Trastuzumab deruxtecan (Enhertu) is an antibody drug conjugate. Pertuzumab (Perjeta) is a newer generation breast cancer drug not currently facing competition.

Competition is highly concentrated in all but one molecule-market where the molecule is facing biosimilar competition

Exhibit 6: Herfindahl-Hirschman Index of Market Concentration and Shares by Competitor, Q2 2020



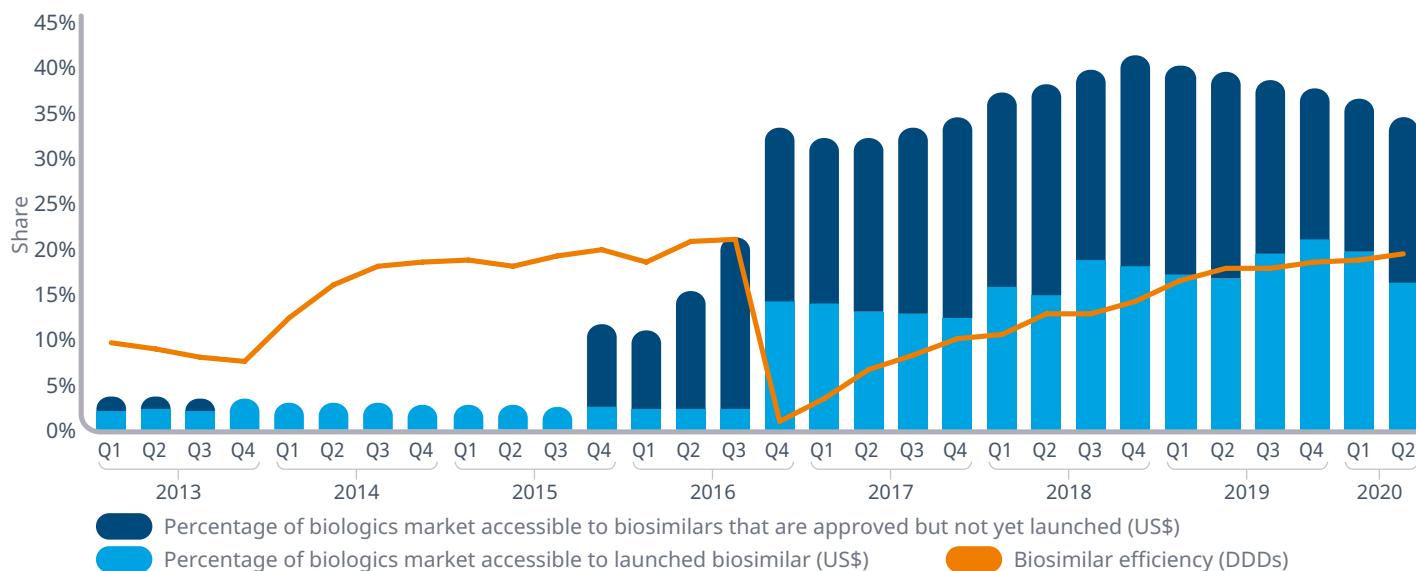
Source: IQVIA National Sales Perspectives, Jun 2020

- As stakeholders consider the impact of biosimilar competition, a common measure of competitiveness in a market is the Herfindahl-Hirschman Index (HHI), which assesses the number of competitors (including the originator) and the market share each achieves, to provide a more nuanced view of market dynamics.
- In sustainable competitive markets, more competitors divide the market more evenly, achieving a low HHI score, while monopolies have a score of 1.0.
- For molecules with biosimilar competition, their HHI scores range from 0.32 to 0.83, with all but one above 0.5 (filgrastim, 0.32). Filgrastim has the lowest concentration of share across the four competitors, suggesting it is currently the most sustainable market.
- Insulin lispro has the highest HHI score (0.83), as there is only one biosimilar competitor, and the originator launched an authorized generic, effectively blunting biosimilar uptake.
- At present, third-or-later biosimilar entrants rarely achieve high volume share, while in other pharmaceutical contexts, competition and price deflation are greatest when there are three or more competitors.
- In the future, deflationary effects on pricing may still be driven by third-or-later entrants, as they may seek more aggressive contracting and discounting to capture share, thereby increasing competitive sustainability if they are successful.
- Longer-term biosimilar savings will be limited if fewer molecules attract large numbers of competitors.

Exhibit Notes: The Herfindahl-Hirschman Index (HHI) is defined as the sum of the squares of market shares. Calculations are based on defined daily dose shares where each medicine is normalized to a standardized dose per day to adjust for formulation differences between originators and biosimilars. Authorized generics are those medicines marketed or authorized by the originator using non-proprietary naming but are the same as the originator product.

Biosimilars launched to date account for 20% of competitive molecule volume

Exhibit 7: Percentage of Biologics Sales Accessible to Approved and Launched Biosimilars and Biosimilar Efficiency, 2013–2019



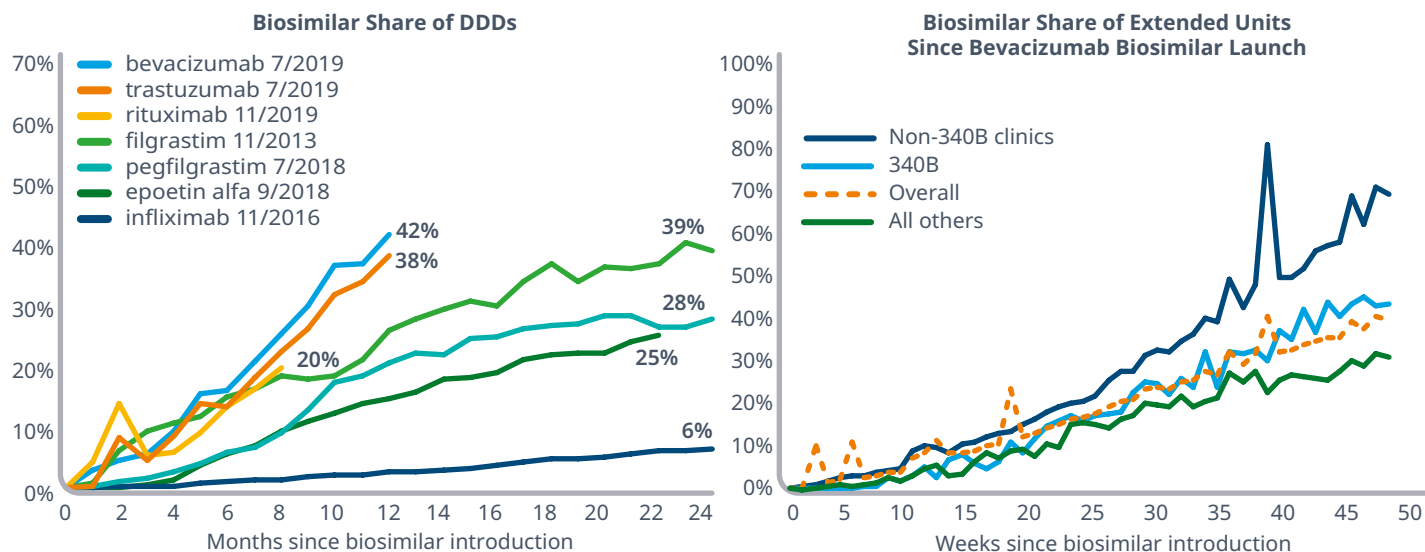
Source: IQVIA National Sales Perspectives, Jun 2020

- Biologic sales currently accessible to and facing biosimilar competition account for 19% of total invoice-level biologic sales (light blue columns), and biosimilar efficiency — meaning the percentage that biosimilars comprise of accessible molecule volume — has reached 20%.
- The potential savings that biosimilars may bring to healthcare stakeholders is often delayed, as is competition, since the approval of biosimilars does not result in their immediate launch. Delays in availability are often due to patent litigation, settlements, and other logistical issues.
- Biosimilars that are approved but not yet launched represent an additional 17% of total invoice-level biologic sales, indicating up to 36% of biologic sales would be exposed to biosimilar competition when they eventually launch.
- The launch of insulin glargine and infliximab biosimilars in 2016 resulted in a significant rise in the accessible market — from 2% to 14% within the first quarter — and reduction in biosimilar efficiency from 21% to 1% until uptake of biosimilars increased.
- The share of the market still potentially accessible to future biosimilars has been declining, as biosimilars launch and medicines transition into the accessible market at lower prices.

Exhibit Notes: See Definitions page for IQVIA Institute definition of biosimilar. Biosimilars that have not been approved as of June 2020 have not been included. FDA approved enoxaparin via the standard generic pathway as an ANDA and also does not consider it a biosimilar. Biosimilar efficiency measures biosimilar share of market volume where biosimilars are approved and launched and for this exhibit is determined by calculating Defined Daily Doses, DDD (see Definitions page).

Recent biosimilars have achieved high volume shares, projected to reach more than 50% within the first two years, varying by channel

Exhibit 8: Biosimilar Share of Volume Since Biosimilar Launch



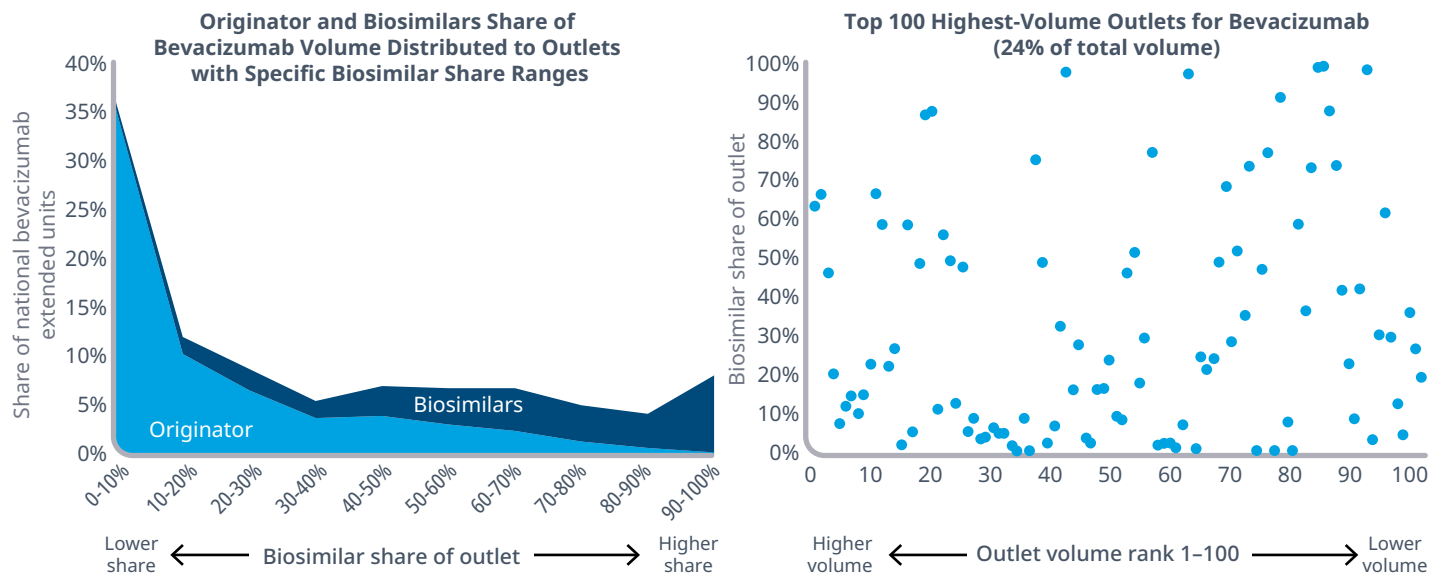
Source: IQVIA MIDAS®, Jun 2020

- The three most recently-launched biosimilars in 2019 have achieved significant uptake within their first year: bevacizumab (42%), trastuzumab (38%), and rituximab (20%). These biosimilars are tracking towards more than 50%, or nearly 60%, by the end of two years on the market — substantially higher than prior biosimilars and similar to the high rates of adoption in Europe.^{4,5,6}
- Earlier biosimilars, such as filgrastim, achieved a 25% share of molecule volume within the first year, and 39% after two years. Notably, after six years on the market, biosimilar filgrastim share has reached 80% (see Exhibit 5).
- Infliximab has had the lowest biosimilar uptake (6%) as a result of competitive dynamics between the originator and biosimilars.
- Bevacizumab has the highest biosimilar share to date, with two competitors gaining 42% share within 12 months.
- The bevacizumab biosimilars achieved substantially higher share in outlets not eligible for 340B discounts, which may be the result of a strategic approach by biosimilar companies to prioritize contracting with those outlets.
- As 2020 has progressed, uptake in 340B has continued to rise, contributing to lower spending as these institutions are entitled to significant discounts on all of their drug purchases.
- The success of recent biosimilars suggests biosimilar competitors have refined their approach to be competitive in the market at launch.

Exhibit Notes: See Definitions page for IQVIA Institute definition of Defined Daily Dose (DDD). Bevacizumab share in right chart is extended unit shares without days of therapy normalization, resulting in differences in overall share compared to DDD-based calculations.

Many providers are using a biosimilar of bevacizumab more than the originator, with significant diversity in these patterns

Exhibit 9: Use of Biosimilars and Originator Bevacizumab Within Outlets



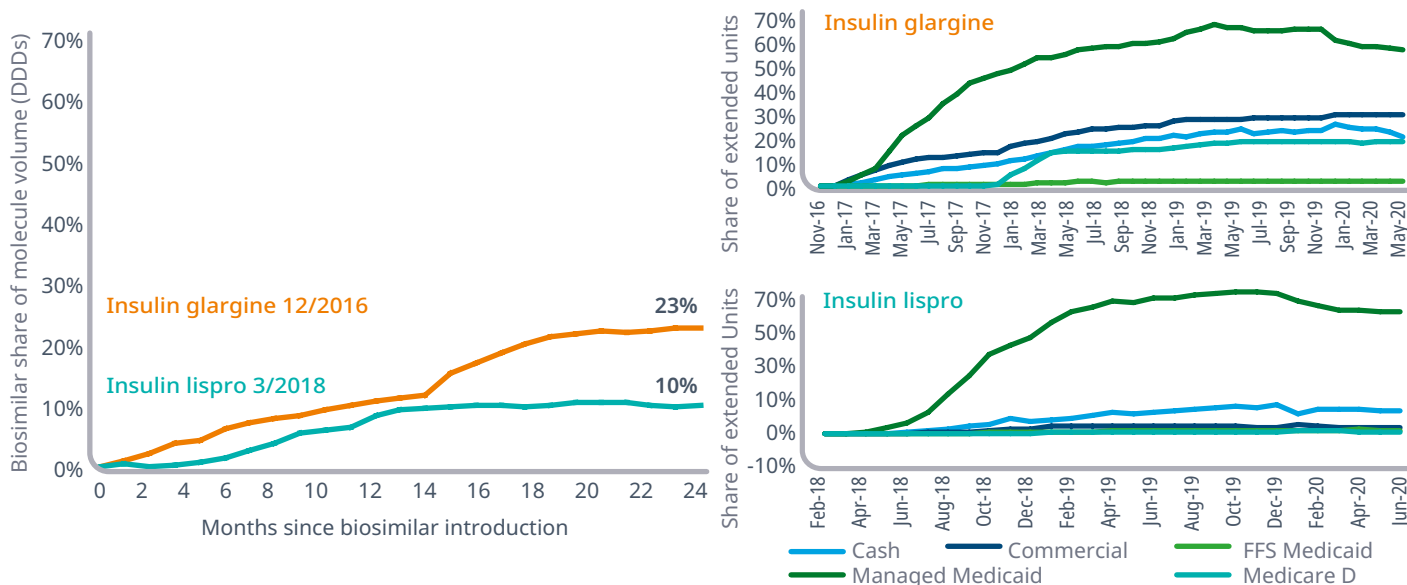
Source: IQVIA DDD, Aug 2020

- Bevacizumab biosimilars have had the highest biosimilar uptake trajectory since the launch of any biosimilar in the United States, yet there is significant variability in their use by providers.
- Among the top 100 provider groups accounting for 24% of overall bevacizumab volume, biosimilar use is highly heterogeneous, ranging from 0–100% of their total bevacizumab use to date in 2020.
- High biosimilar use is not correlated with the overall volume of bevacizumab used by the outlets, with some large outlets avoiding having to manage switching of non-interchangeable products by treating with only a biosimilar or the originator, while the majority of providers are using both, though the extent of switching is not yet clear.
- Many providers use biosimilars very sparingly or not at all, with 37% of bevacizumab volume going to providers that use biosimilars less than 10% of the time, including 14% who use no biosimilars (not shown).
- Overall, 70% of biosimilar volume goes to outlets using biosimilars more than 50% of the time.
- It is expected that, over time, more outlets will begin to use biosimilars and use them more often, contributing to an expected rise of biosimilar share to 50% or greater by mid-2021, two years after initial bevacizumab biosimilar launch (see Exhibit 8).

Exhibit Notes: Outlet biosimilar shares and volume calculated using YTD Aug 2020 data. Data from outlet level data, details such as name location are confidential. Top 100 combines corporate parents and excludes multi-doctor/practice group purchasing organizations.

Biosimilar penetration at pharmacies is influenced by insurance type and competitive actions by the originating company

Exhibit 10: Insulin Biosimilars Share of Molecule Volume, Since Launch and by Method of Payment



Source: IQVIA MIDAS®; IQVIA SMART Managed Care, Jun 2020

- Patient access to and uptake of biosimilars may vary based on incentives of various stakeholders. In the case of pharmacy-reimbursed drugs such as these, pharmacy benefit managers (PBMs) are the key stakeholder in the negotiation of formularies and/or rebates, and may prefer either biosimilar or originators for financial reasons.
- In the only two examples of PBM-reimbursed drugs, the uptake of insulin glargine and insulin lispro have differed greatly with the former reaching a 23% share of molecule volume and the latter 10%. However, these do not differ drastically from biosimilar uptake of medical-benefit reimbursed drugs (see Exhibit 8).
- These two biosimilars have seen drastically different uptakes based on insurance type, with both insulin products reaching 68% uptake in Managed Medicaid by the end of 2019. This is likely due to the incentive structures governing Managed Medicaid, where the

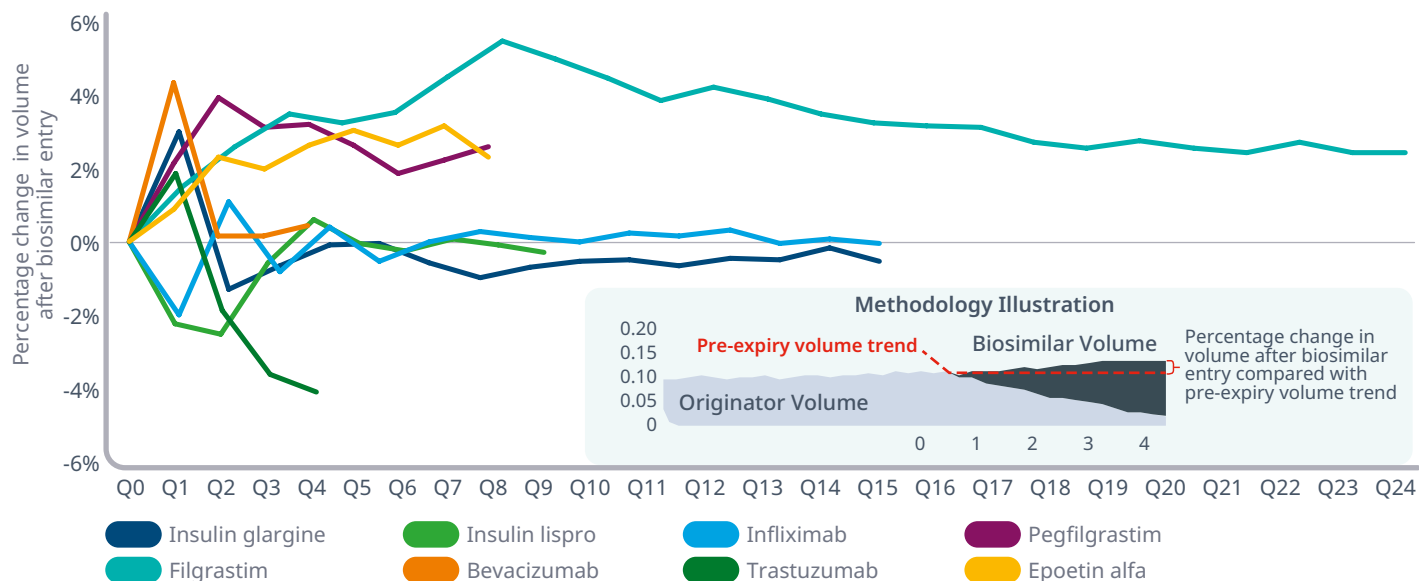
outsourced commercial managers retain a share of manufacturer rebates.

- The insulin glargine biosimilar launched in December 2016, but was not included on the Medicare Part D formularies until January 2018, reflecting the difficulty of penetrating some insurance pay types. Similarly, in the commercial channel, the biosimilar has only achieved 30% share of volume, though there was early uptake in the channel.
- Biosimilar insulin lispro faced an additional obstacle as the originator launched an ‘authorized generic’ with a lower cost than the brand (likely without confidential rebates), which was attractive to some plans where patient price sensitivity was an issue.
- In this way, the originator was able to negotiate effectively with both brand rebates and authorized generics to effectively blunt biosimilar volume gains.

Exhibit Notes: Overall biosimilar volume share in defined daily doses (DDD) on the left chart assumes 40 IU per day for insulin products. Method of payment volume shares are based on extended units (EU), in this case a measure of the pre-filled pens that are typically sold in a 5-pack, the most common form of therapy normalization, resulting in differences in overall share compared to DDD-based calculations.

Biosimilars have generated incremental demand for molecules without newer-generation medicines in the market

Exhibit 11: Incremental Volume after Biosimilar Entry Compared to Prior Trend



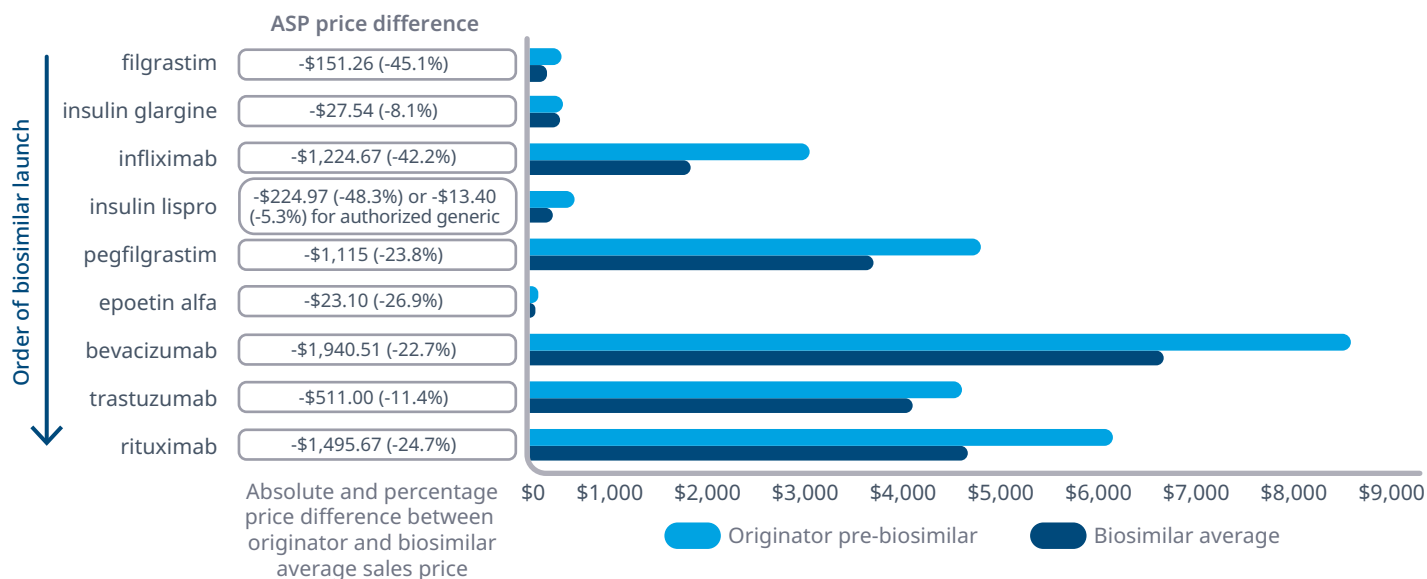
Source: IQVIA MIDAS®, Jun 2020; IQVIA Institute, Sep 2020

- Biosimilars represent the potential for significant savings, while also offering increased access to cost-sensitive patients. As a result, whole molecule volume is expected to grow when biosimilars are introduced. Comparisons between the molecule volume trend pre- and post-biosimilar entry indicate there are complex dynamics at play.
- As biosimilars become available, some molecules have seen nearly 5% incremental volume (e.g., filgrastim).
- Molecules that have seen sustained increases in volume are oncology supportive care medications — potentially due to cost-sensitive patients returning to treatment — or patients on other medicines in the same classes being treated with a new molecule.
- In the case of filgrastim and pegfilgrastim, there is a clear pattern of incremental volume shifting to the cheaper and shorter-acting filgrastim until 2018, when pegfilgrastim biosimilars became available (see Exhibit 5).
- Notably, insulin lispro and infliximab have seen no appreciable increases in incremental volume, and they notably have more concentration in their HHI index (see Exhibit 6). Taken together, this suggests that competitive dynamics for these molecules may be less sustainable for biosimilars.
- Some medicines, like bevacizumab and trastuzumab, have shown short-term increases in volume, but lack a sustained trend to date.

Exhibit Notes: Volume is based on a defined daily dose (DDD). Pre-expiry volume trend is based on three years prior to biosimilar entry. Change in volume is calculated comparing the molecule total volume to the expected volume from the pre-expiry trend.

Absolute savings from biosimilars vary, with larger savings from more recent launches where originators were more costly

Exhibit 12: Originator and Mean Biosimilar Average Sales Price (ASP) in US\$, July 2020



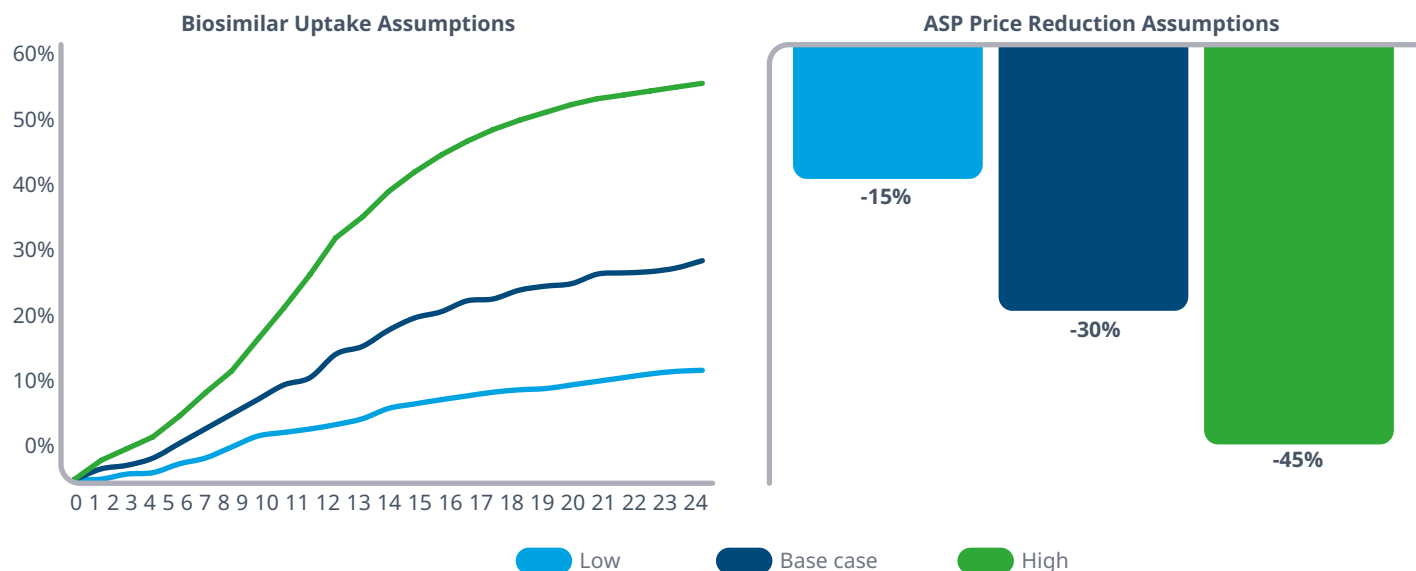
Source: CMS ASP Jul 2020 accessed Sep 2020; IQVIA National Sales Perspectives, Jul 2020; IQVIA Institute, Sep 2020

- The three most recent biosimilars launched in 2019, bevacizumab, trastuzumab, and rituximab, have seen ASP price reductions of \$500–\$1,900 for a standard course of treatment, potentially a factor in the high uptake of these biosimilars.
- As ASP-based reimbursement is used in Medicare Part B and in some commercial plans, this analysis shows an ASP cost comparison as an indicator of the burden and/or savings biosimilars offer to payers. Though patient cost-sharing models differ, patients typically pay 20% of Medicare costs.
- For pharmacy products, average invoice prices are often closest to the price patients pay during their deductible, notwithstanding pharmacy markups.
- Since insulin glargine biosimilar Basaglar launched, costs at invoice prices have declined only 8%, meaning patients have saved less to date from the advent of biosimilar insulins compared with biosimilars for other molecules.
- The price of the insulin lispro biosimilar, Admelog, is 45% less than its originator, Humalog, and the originator-manufactured ‘authorized generic’ is only 5% more expensive than the biosimilar, bringing two lower-cost options to plans and patients.
- Medicare and commercial patients save an average of \$17 per prescription when using a biosimilar insulin, with Medicare paying on average \$18–19 and commercial patients paying \$13–14.*

Exhibit Notes: Average sales price (ASP) costs have been normalized to standardized dosing for each medicine to calculate comparable costs. Insulins use IQVIA invoice prices. ASP for biosimilars was calculated from the CMS website using July 2020 values and period pre-biosimilar entry for each medicine as accessed September 2020: filgrastim 5mcg/kg, insulin glargine, and insulin lispro 5-pen pack 100units/ml 3ml, infliximab 5mg/kg, pegfilgrastim 6mg per chemotherapy cycle, epoetin alfa 100 units/kg, bevacizumab 15mg/kg, trastuzumab 6mg/kg, rituximab 375mg per meter-squared body surface area. Standard body weight was considered 70kg and standard body surface area 1.7 meters squared. *IQVIA Institute LAAD data.

Volume uptake scenarios include high, medium and low, tied to both originator competition and price reductions ranging from 15 to 45%

Exhibit 13: Modeling of Scenarios based on Average (Base Case), High and Low Examples to Date



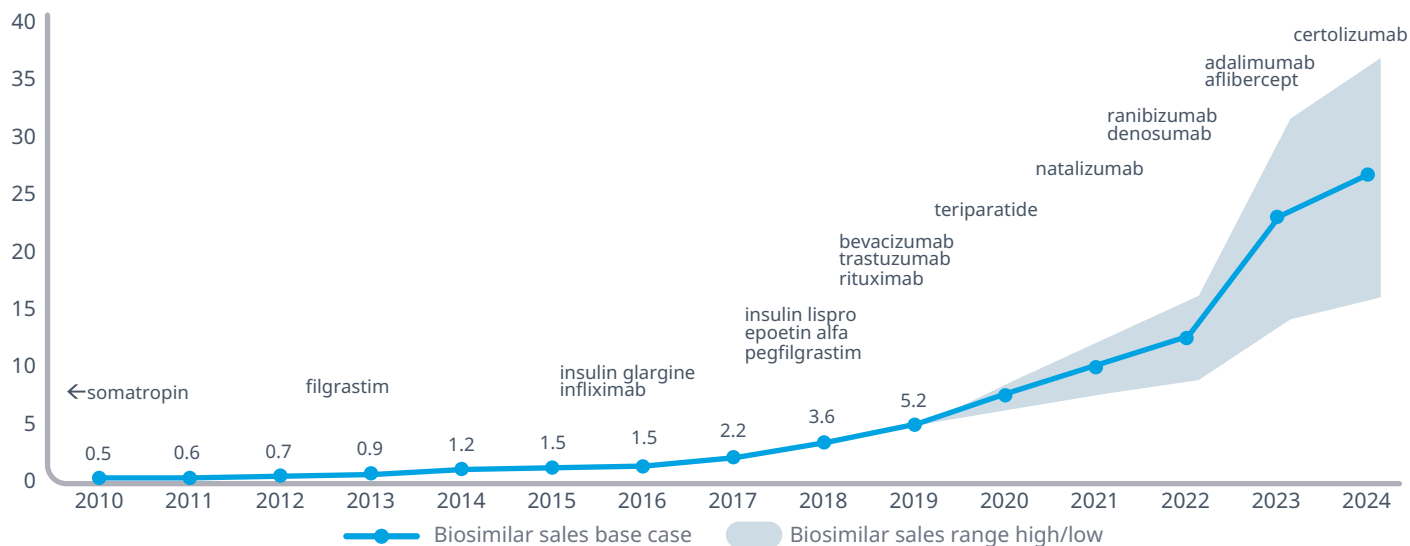
Source: IQVIA Institute, Sep 2020

- Future biosimilar sales and savings will depend on the market dynamics and behaviors of competing companies, their negotiations with payers, and the actions of patients and healthcare providers.
- The base case scenario used for future projections estimates a 30% biosimilar share of molecule volume is achieved after 24 months along with a 30% price reduction compared to the originator. Notably, this corresponds to the average historical biosimilar uptake and aligns with estimates by many observers.
- A low volume uptake scenario (15% share at 24 months) could occur if originator and biosimilar challengers find that conceding less in discounts (15%) makes available a smaller but more profitable market segment.
- Low volume uptake could also occur if providers and patients are wary of using biosimilars, or if originator marketers aggressively defend their positions, through strategies including authorized generics.
- Higher uptake (55% share at 24 months) is more likely associated with aggressive discounting (e.g., a 45% price reduction), though the overall spending level on a medicine could make even small discounts attractive to payers.
- These scenarios represent the variety of market dynamics expected in the future, with some molecules attracting more biosimilars who then offer aggressive discounting, while other molecules may attract fewer competitors with less aggressive strategies. Depending on market opportunity, some molecules may not attract competitors at all.

Exhibit Notes: High, low, and base case assumptions of biosimilar uptake in terms of volume and price discounts relative to originators are based on IQVIA Institute analysis of historic analogues.

Expected launches and uptake are likely to increase overall spending on biosimilars significantly to \$16–36 billion by 2024

Exhibit 14: Biosimilar Historical Sales 2010–2019 and Outlook Scenarios 2020–2024, US\$Bn



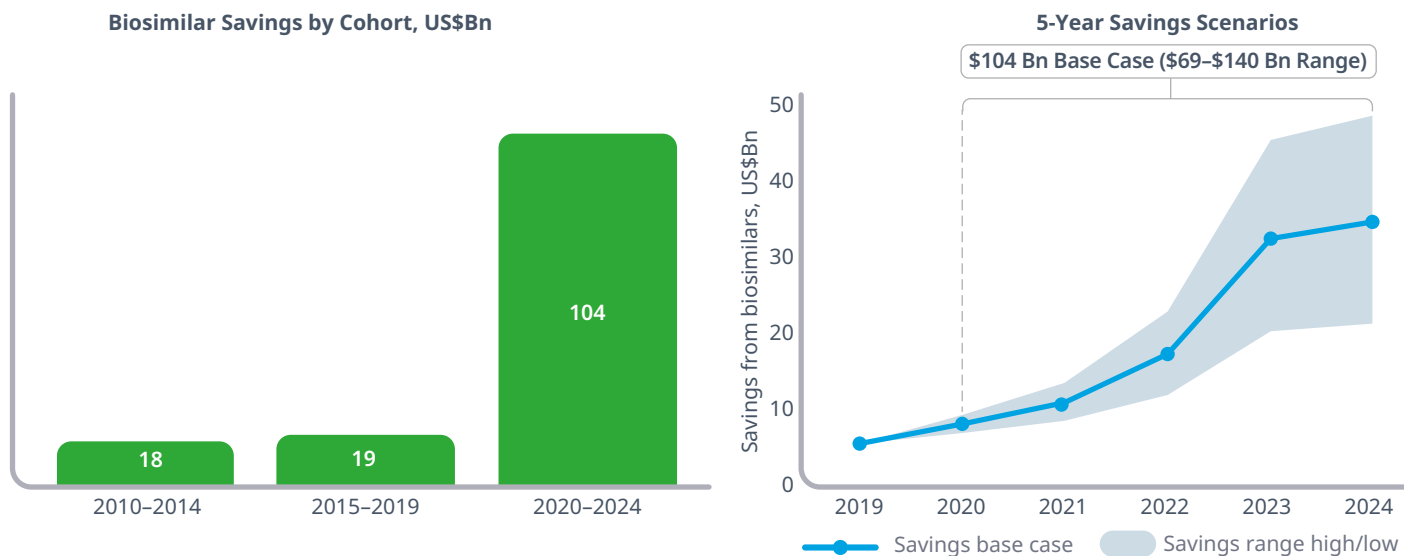
Source: IQVIA National Sales Perspectives Jun 2020; IQVIA Institute, Sep 2020

- Biosimilar sales over the next five years are expected to total \$80 billion, ranging from \$53 to \$105 billion depending on volume uptake and pricing discounts.
- In the next five years, at least seven molecules will face biosimilar competition for the first time in the United States, including some of the highest-selling medicines like adalimumab.
- Biosimilar spending of \$5.2 billion in 2019 is expected to rise to nearly \$27 billion in 2024 in the base case, with scenarios ranging from \$16 to \$36 billion.
- As historical experience is an imperfect guide to future market dynamics, these scenarios represent a range of potential outcomes, and varied market dynamics are possible in each molecule’s market.
- Each biologic medicine is attracting different numbers of competitors (see Exhibit 3), each potentially pursuing more or less aggressive strategies, and facing originators who may or may not compete to defend their market position.
- As an example, the three molecules facing 2019 biosimilar entry (bevacizumab, trastuzumab, and rituximab) share the same originator manufacturer (Roche/Genentech), and all have a similar trajectory of challenger uptake, likely to exceed 50% by the end of two years (see Exhibit 8).
- In contrast, earlier expiries in the past five years have had half-as-much uptake (see Exhibit 8), with fewer biosimilar competitors and greater originator defense.

Exhibit Notes: Historical values are from IQVIA audits, and values for 2020–2024 are based on modeling of expected impact of in-progress biosimilar events and projected future events. The range of biosimilar sales values shown in the outlook scenarios reflect assumptions for high, low, and average (base case) biosimilar volume uptake and price discounts relative to originators. Timing of expected biosimilar entry based on patent information and litigation/settlements as of June 2020.

Savings over the next five years as a result of biosimilars are projected to exceed \$100 billion, though uncertainties remain

Exhibit 15: Biologic Estimated Savings from Biosimilars at Invoice Prices



Source: IQVIA National Sales Perspectives, Jun 2020; IQVIA Institute, Sep 2020

- In the 10 years since the passage of the Biosimilars Act (BPCIA),⁷ \$17 billion of biosimilar spending was associated with savings of \$37 billion compared to what spending would have been without biosimilars.
- The next five years are expected to result in an almost five-fold increase in savings relative to the past five years, as newly approved biosimilars launch, and existing biosimilars see continued uptake and price reductions.
- The most impactful biosimilars in the next five years — those referencing adalimumab — will first appear in 2023 as a result of negotiated patent litigation settlements. As they reach the market, with five already approved (see Exhibit 3), patients will undoubtedly benefit from lower costs to receive the world’s current top-selling biopharmaceutical.
- In addition to new biologic molecules facing biosimilars from 2020–2024, the recent group of biosimilars approved and launched in 2018 and 2019 are continuing to generate substantial savings as uptake increases and prices decline.
- Market events to date suggest a wide range of market outcomes are still possible, ranging from lower biosimilar volume with lower discounts to higher Europe-like volume shares, and bigger discounts.^{5,6}

Exhibit Notes: Historical savings were calculated by comparing actual molecule spending to projected spending if total molecule volume had been at originator pre-expiry prices. Projected future savings based on estimated continuing impact of biosimilar events in progress, as well as future expected expiries. The range of savings values shown in the biosimilar savings scenarios include assumptions for high, low, and average (base case) biosimilar volume uptake and price discounts relative to originators.

Notes on sources

The trends presented reflect United States activities only.

THIS REPORT IS BASED ON THE IQVIA SERVICES DETAILED BELOW

NATIONAL SALES PERSPECTIVES® (NSP) measures revenue within the U.S. pharmaceutical market by pharmacies, clinics, hospitals and other healthcare providers. NSP reports 100% coverage of the retail and non-retail channels for national pharmaceutical sales at actual transaction prices. The prices do not reflect off-invoice price concessions that reduce the net amount received by manufacturers.

MIDAS® is a unique platform for assessing worldwide healthcare markets. It integrates IQVIA's national audits into a globally consistent view of the pharmaceutical market, tracking virtually every product in hundreds of therapeutic classes and provides estimated product volumes, trends and market share through retail and non-retail channels. MIDAS® data is updated monthly and retains 12 years of history. U.S. data in MIDAS® are derived from National Sales Perspectives but include some alternative segmentation and reporting options that were employed in this report including biologic and biosimilar reference fields.

IQVIA DRUG DISTRIBUTION DATA® (DDD)

IQVIA DDD or Sub-National Outlet-Level Sales, combines direct shipments from manufacturers and wholesalers to retail and non-retail purchasers, to provide outlet-level data. Data are provided by participating companies and wholesalers and pooled and blinded to limit contributors to viewing granular data for their own products and summarized results for others. Outlet level analysis in this report is further blinded to mask the specific outlets and products consistent with IQVIA contractual obligations with data providers.

IQVIA'S NATIONAL PRESCRIPTION AUDIT (NPA)

NPA is the industry standard source of national prescription activity for all pharmaceutical products. It measures demand for prescription drugs, including dispensed pharmaceuticals to consumers across three unique channels: retail, mail service, and long-term care pharmacies. From sample pharmacies, IQVIA collects new and refilled prescription data daily. NPA represents and captures over 92% of all outpatient prescription activity in the United States and covers all products, classes, and manufacturers.

IQVIA'S NATIONAL PRESCRIPTION AUDIT: MANAGED CARE

IQVIA Managed Care combines NPA with segmentation of a patient's methods of payment for pharmacy transactions.

IQVIA PIPELINE INTELLIGENCE is a drug pipeline database containing up-to-date R&D information on over 40,000 drugs, and over 9,000 in active development worldwide. The database captures the full process of R&D, covering activity from discovery stage through preclinical and clinical development, to approval and launch.

IQVIA'S LONGITUDINAL PRESCRIPTION DATA

IQVIA receives nearly four billion prescription claims per year with history from January 2006, and covers over 90% of the retail channel, 60–85% of mail service, and 75–80% of long-term care. Longitudinal data derives from electronic data received from pharmacies, payers, software providers and transactional clearinghouses. This information represents activities that take place during the prescription transaction and contains information regarding the product, provider, payer, and geography. Rx data is longitudinally linked back to an anonymous patient token and is linkable to events within the dataset itself and across other patient data assets.

Definitions



Biologic: IQVIA defines biologic medicines as complex macromolecules such as proteins, nucleic acids and carbohydrates. They must be clearly identified with specific molecule name(s), and exclude more general descriptions such as ‘vegetable extract’. Fixed combinations of biologic and small molecule products are considered biologic. The biologic substance must have undergone (or be undergoing) a regulatory trial program under the auspices of a regional regulatory authority. FDA changes to categorization of biologics and biosimilars in March 2020 bring their definitions more in line with those used here.

Biosimilar: a non-original biologic medicine produced through recombinant technology and approved through an abbreviated pathway. In the United States the Biologics Price Competition and Innovation Act 2009 (BPCIA) created the 351(k) pathway for biosimilars, however some products were approved through the 505(b)(2) pathway for abbreviated approvals of non-original products referencing another product in the submission. Others were submitted as a BLA or original biologics license application under the 351(a) pathway. Both approaches occurred either prior to the implementation of the 351(k) pathway or because the manufacturer chose to submit their regulatory dossier via the alternative approach.

Developer: The company that has made the initial clinical research and/or regulatory filings

Marketer: The company selling the product in the market, either having licensed the product from the developer or having acquired the asset or company through a merger or other acquisition.

Herfindahl-Hirschman Index: The Herfindahl index is a measure of the size of firms in relation to the industry and an indicator of the amount of competition among them. Named after economists Orris C. Herfindahl and Albert O. Hirschman, it is an economic concept widely applied in competition law, antitrust and also technology management. It is calculated as the sum of the squares

of the market share of each market participant, with monopoly situations resulting in an index of 1.0 and multiple evenly distributed competitors approaching but never reaching zero.

Accessible market: the total of biosimilars and the originators they are similar to, measurable in volume or spending terms.

Biosimilar efficiency: The biosimilar share of the accessible market.

Defined Daily Dose (DDD): The World Health Organization normalized measure of a day of therapy using standardized dosing assumptions. *Note: this is unrelated to IQVIA's Drug Distribution Data offering, also named DDD.*

Extended Units (EU): an IQVIA defined measure of volume. Each extended unit represents a dosage form of a medicine, where the specific definition varies by the type of formulation. A pill or a pre-filled vial, or an injection pen are each equal to one EU. For some forms an EU is a number of milligrams or milliliters. Extended units of dissimilar forms should not be combined for analytical purposes.

Invoice Price: Invoice-based pricing is defined as sales volumes reported at the invoice prices between manufacturers and their customers as reported in MIDAS®, notably different by ~4% from prices in IQVIA National Sales Perspectives, which are used in the IQVIA Institute report, *Medicine Spending and Affordability in the United States*.²

Average Sales Price (ASP): Manufacturers average sales price to all purchasers excluding Medicaid and certain federal discounts or rebates. ASP does not reflect separately negotiated discounts and rebates with insurers or pharmacy benefit managers.

Biosimilar Savings: the amount of spending lower than what would have been spent if all volume had been at originator pre-biosimilar prices.

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Murray Aitken is Executive Director, IQVIA Institute for Human Data Science, which provides policy setters and decisionmakers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics, now the IQVIA Institute, since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health's thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company's consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.

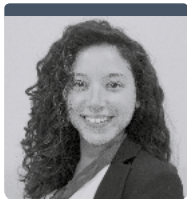


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Research Director, IQVIA Institute
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Michael Kleinrock serves as research director for the IQVIA Institute for Human Data Science, setting the research agenda for the Institute, leading the development of reports and projects focused on the current and future role of human data science in healthcare in the United States and globally. Kleinrock leads the research development included in Institute reports published throughout the year. The research is focused on advancing the understanding of healthcare and the complex systems and markets around the world that deliver it. Throughout his tenure at IMS Health, which began in 1999, he has held roles in customer service, marketing, product management, and in 2006 joined the Market Insights team, which is now the IQVIA Institute for Human Data Science. He holds a B.A. degree in History and Political Science from the University of Essex, Colchester, UK, and an M.A. in Journalism and Radio Production from Goldsmiths College, University of London, UK.

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Elyse Muñoz is a Thought Leadership Manager for the IQVIA Institute, managing aspects of IQVIA Institute research projects and conducting research and analysis within global healthcare. Elyse joined IQVIA in 2017 as an associate consultant in the Competitive Intelligence consulting group, where she developed rich clinical and commercial insights to serve million-dollar clients. She worked in major therapy areas including diabetes, cardiovascular disease and kidney dysfunction, as well as rare diseases such as hemophilia. Elyse holds a Bachelor of Science from Arizona State University in genetics, as well as a Ph.D. in genetics from Pennsylvania State University. Her research focused on understanding the genetic makeup of the parasite which causes malaria to aid in targeted drug development to help eradicate the disease.

About the Institute



The IQVIA Institute for Human Data Science contributes to the advancement of human health globally through timely research, insightful analysis and scientific expertise applied to granular non-identified patient-level data.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision making and improved human outcomes. With access to IQVIA's institutional knowledge, advanced analytics, technology and unparalleled data the Institute works in tandem with a broad set of healthcare stakeholders to drive a research agenda focused on Human Data Science including government agencies, academic institutions, the life sciences industry and payers.

Research Agenda

The research agenda for the Institute centers on 5 areas considered vital to contributing to the advancement of human health globally:

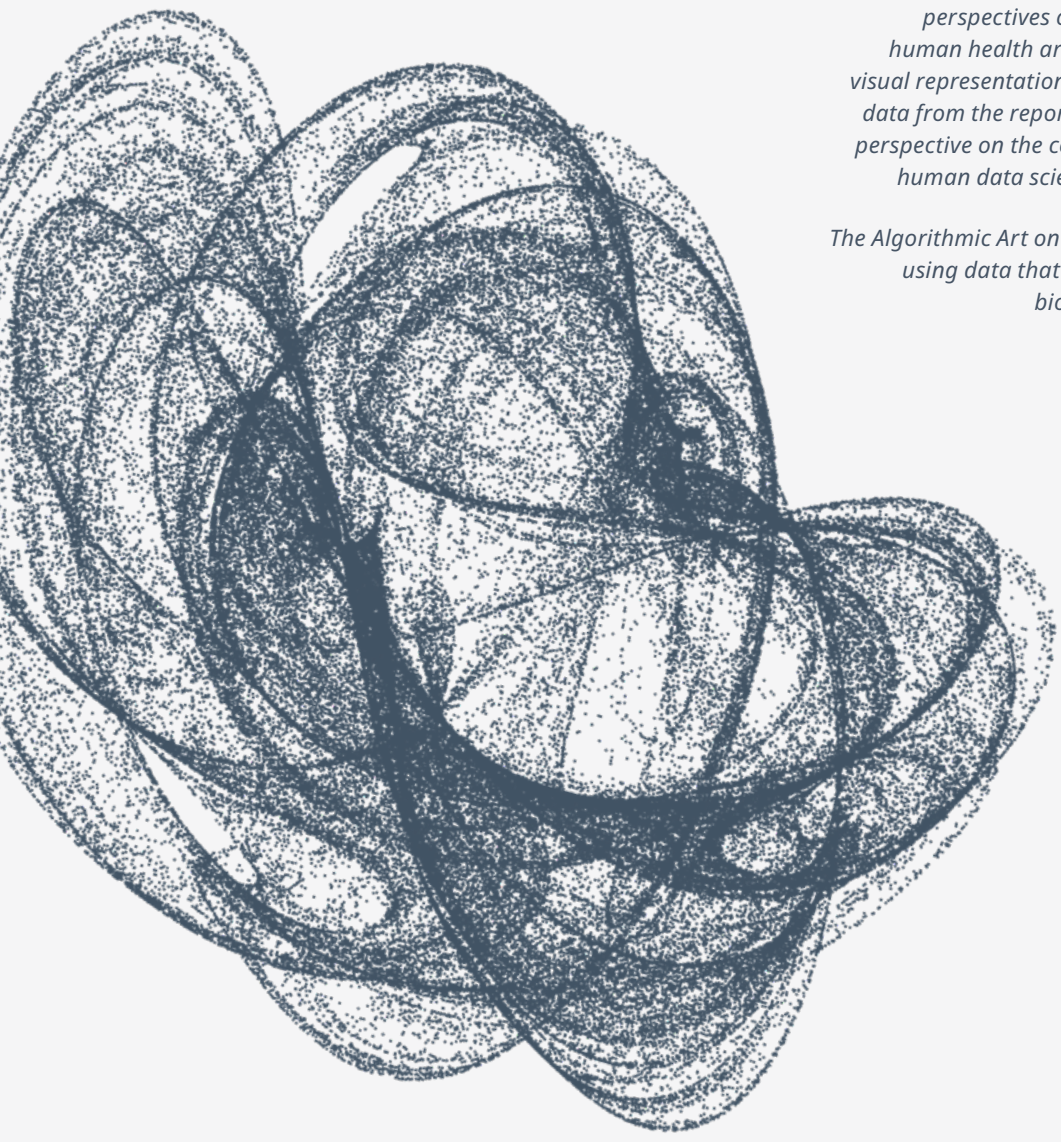
- Improving decision-making across health systems through the effective use of advanced analytics and methodologies applied to timely, relevant data.
- Addressing opportunities to improve clinical development productivity focused on innovative treatments that advance healthcare globally.
- Optimizing the performance of health systems by focusing on patient centricity, precision medicine and better understanding disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.

- Understanding the future role for biopharmaceuticals in human health, market dynamics, and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of technology in health system products, processes and delivery systems and the business and policy systems that drive innovation.

Guiding Principles

The Institute operates from a set of guiding principles:

- Healthcare solutions of the future require fact based scientific evidence, expert analysis of information, technology, ingenuity and a focus on individuals.
- Rigorous analysis must be applied to vast amounts of timely, high quality and relevant data to provide value and move healthcare forward.
- Collaboration across all stakeholders in the public and private sectors is critical to advancing healthcare solutions.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Protecting individual privacy is essential, so research will be based on the use of non-identified patient information and provider information will be aggregated.
- Information will be used responsibly to advance research, inform discourse, achieve better healthcare and improve the health of all people.



The IQVIA Institute for Human Data Science is committed to using human data science to provide timely, fact-based perspectives on the dynamics of health systems and human health around the world. The cover artwork is a visual representation of this mission. Using algorithms and data from the report itself, the final image presents a new perspective on the complexity, beauty and mathematics of human data science and the insights within the pages.

The Algorithmic Art on the cover of this report was generated using data that captures sales, volume, and the use of biosimilar and originator products in the United States from 2010-2019.



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