Economic Considerations Related to Biosimilar Market Entry

by Pavel Darling, Andrée-Anne Fournier, and Michael Carson; Analysis Group, Inc.

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Pavel Darling


Andrée-Anne Fournier


Michael Carson

Allegations of delayed generic entry for pharmaceuticals often give rise to antitrust issues. Such matters are typically focused on allegations that actions taken by other marketplace participants delayed the generic entry of small-molecule drugs, which can provide therapeutically equivalent treatment options to branded reference products at potentially lower prices. To promote the use of generics, most states have adopted generic "substitution" laws, which allow or require pharmacists to dispense the generic when available and cheaper. As a result, generics can experience rapid uptake following their introduction.[1]

Like generics, biosimilars are recognized as a means of providing similar treatment options to originator biologics at potentially lower prices. Over the past decade, biologics have become increasingly important in the pharmaceuticals space – for example, as of 2021, nearly half of prescription drug spending in the U.S. was on biologics.[2] While biosimilar competition is still in its early stages, with the first biosimilar having only been approved in March 2015, as of today there are approximately 50 US Food and Drug Administration-approved (FDA-approved) and commercially available biosimilars.[3] Of the $260 billion spent on biologics in the U.S. in 2021, only $38 billion (14 percent) was spent on biologics facing biosimilar competition, while $181 billion (70 percent) was spent on biologics that may face future biosimilar competition.[4] Of the $181 billion, $96 billion

was spent on biologics for which biosimilars were in development as of 2021.[5] Thus, there is a significant potential for further biosimilar competition in the coming years.

As the number of biologics has grown, there has also been an increase in litigation related to competition between originator biologics and biosimilars, such as recent matters pertaining to the originator biologics Stelara and Lantus.[6] Notably, such litigations can impact the timing of biosimilar market entry. For example, the recent litigation for the originator biologic Humira resulted in multiple settlements with staggered U.S. launch dates for adalimumab biosimilars, which has led to allegations of delayed biosimilar entry.[7] Thus, there seems to be a potential movement for biosimilars that is analogous to what has been observed for generics, where settlement agreements over patent litigations are being challenged as anticompetitive, or other business practices are being alleged as anticompetitive and causing delays in competition. Consistent with emerging competition-related litigation for biologics and biosimilars, antitrust agencies are also becoming increasingly focused on competition between originator biologics and biosimilars.[8]

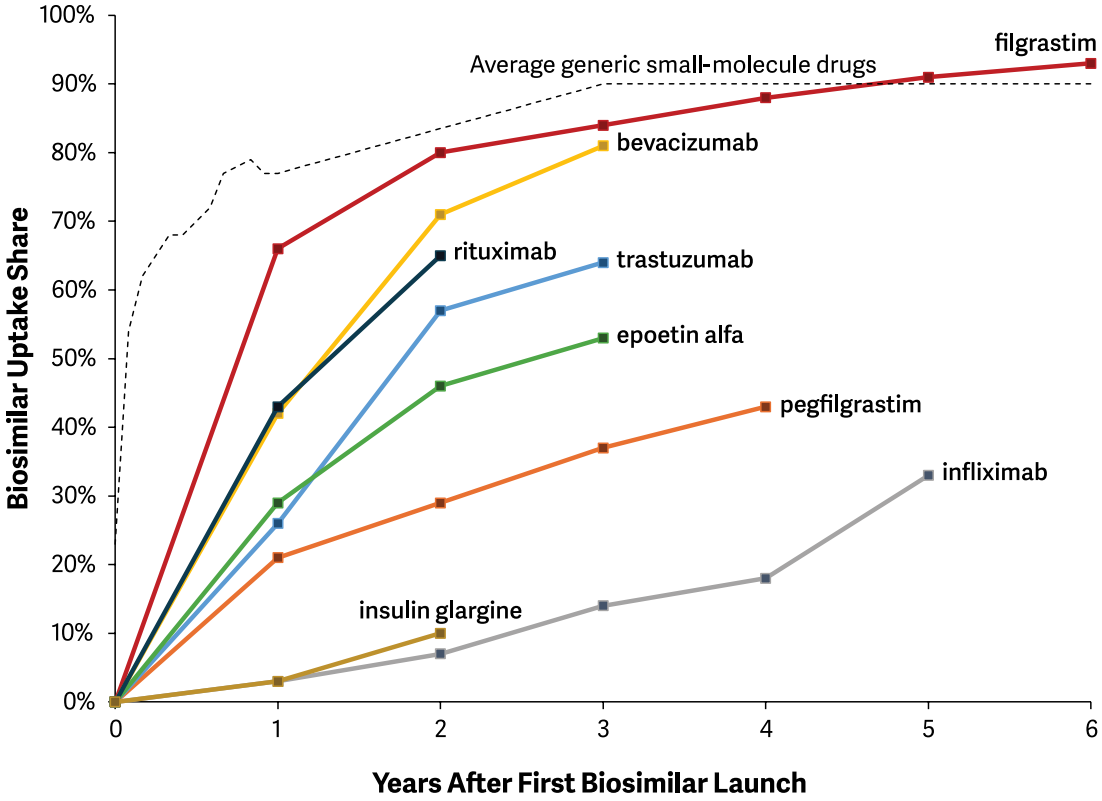
In litigation related to competition between originator biologics and biosimilars, questions around class certification, liability, and/or damages will require both plaintiffs and defendants to rely on assumptions regarding the anticipated uptake of biosimilars following market entry, and the anticipated pricing of biosimilars and originator biologics. While uptake and pricing trends following the introduction of generics has been widely studied (though still debated in the courts), such trends have been less studied for biosimilars. This paper looks to help further such analyses by exploring the uptake- and price-related experience of biologics and biosimilars, and examining how the competitive environments have evolved for different biosimilar entrants.

Economic considerations related to biosimilar market entry

Biosimilar uptake following market entry

Biosimilar uptake in the U.S. has been slower for some biosimilars than for others, and in general at a slower rate than the uptake observed for many generics, as shown in **Figure 1**. For example, researchers found that according to prescription drug data from IQVIA, infliximab biosimilars had achieved a less than 35 percent share five years after the first infliximab biosimilar launched in 2016.[9] Meanwhile, other biosimilars have achieved a higher rate of uptake. For example, bevacizumab biosimilars achieved approximately an 80 percent share only three years after the first biosimilar launched in 2019.[10] In contrast to both of these examples, the uptake of generic small-molecule drugs is often (but not always) characterized by rapid uptake in the first several years. As shown by the dotted line at the top of the figure, generics often achieve approximately 90 percent of the molecule's total dosage quantity just three years after market entry.[11]

Figure 1: Biosimilar uptake post-market entry[12]



Biosimilar uptake varies and is not uniform across molecules

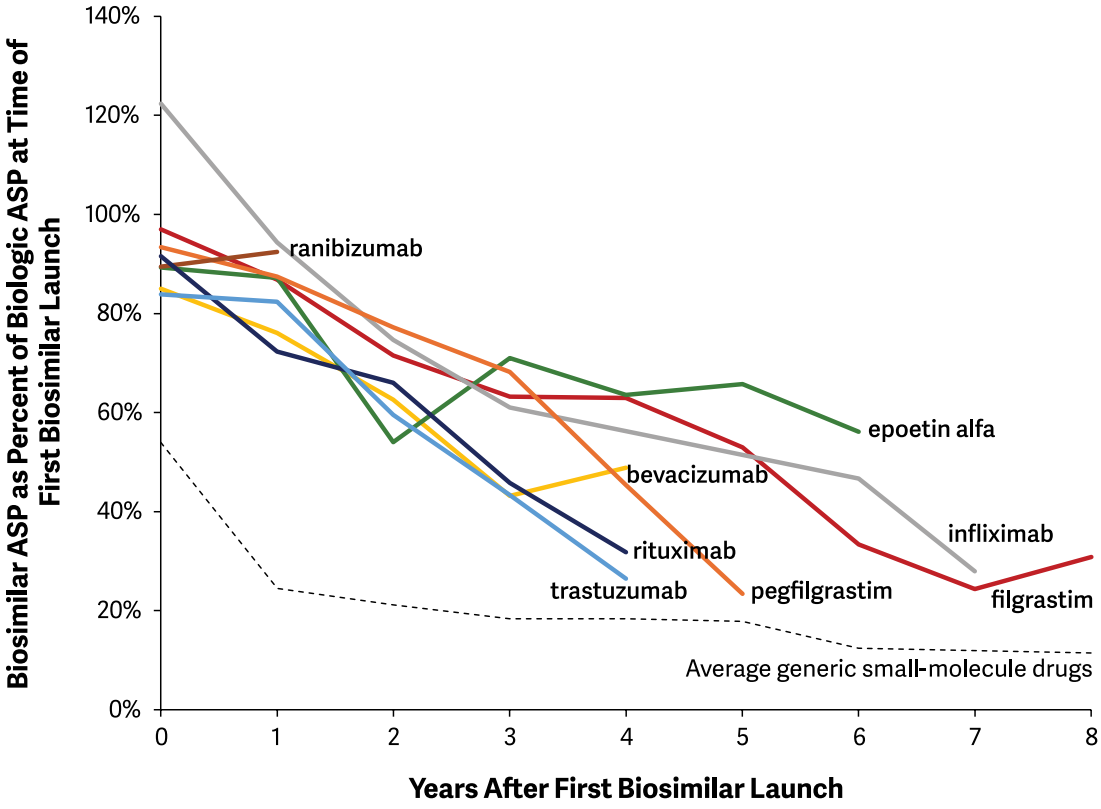
In general, biosimilar uptake has varied across molecules to date. Published literature has assessed potential drivers of this variation in biosimilar uptake. Such potential drivers may include (but are not limited to) the lack of therapeutic equivalence for some biosimilars and the corresponding lack of regulated substitution; physicians' differing familiarity with biosimilars (e.g., certain physicians are specialized in treatment areas for which no biosimilars have yet been approved); and how different conditions are treated (e.g., certain research indicates patients and physicians may be more reluctant to switch to biosimilars for treating chronic conditions).[13] An additional factor that contributes to the often rapid uptake of generics is that such products are often offered at considerably lower prices than branded products.[14] To the extent that price discounts offered by biosimilars have varied, this can also contribute to the differing uptake of biosimilars relative to the uptake of generics.[15]

Biologic and biosimilar prices following biosimilar market entry

As mentioned above, price discounts offered by biosimilars have varied, and further, biologic and biosimilar pricing is not uniform across molecules. This is highlighted in **Figure 2**, which shows biosimilars' prices over time relative to what the prices of originator biologics were just prior to biosimilar entry. For example, according to Centers for Medicare & Medicaid Services (CMS) Medicare Part B average sales price (ASP) data, at five years following the introduction of pegfilgrastim biosimilars, the ASP of these

products was approximately 25 percent of the originator biologic's (Neulasta's) price prior to biosimilar entry. Meanwhile, five years following the introduction of epoetin alfa biosimilars, the ASP of these products was approximately 65 percent of the originator biologic's (Epogen's/Procrit's) price prior to biosimilar entry. In contrast, researchers have found that in just three years following the introduction of generic small-molecule drugs, the price of these products is on average (but not always) approximately 20 percent of the branded product's price prior to generic entry (as shown by the dotted line at the bottom of the figure).[16]

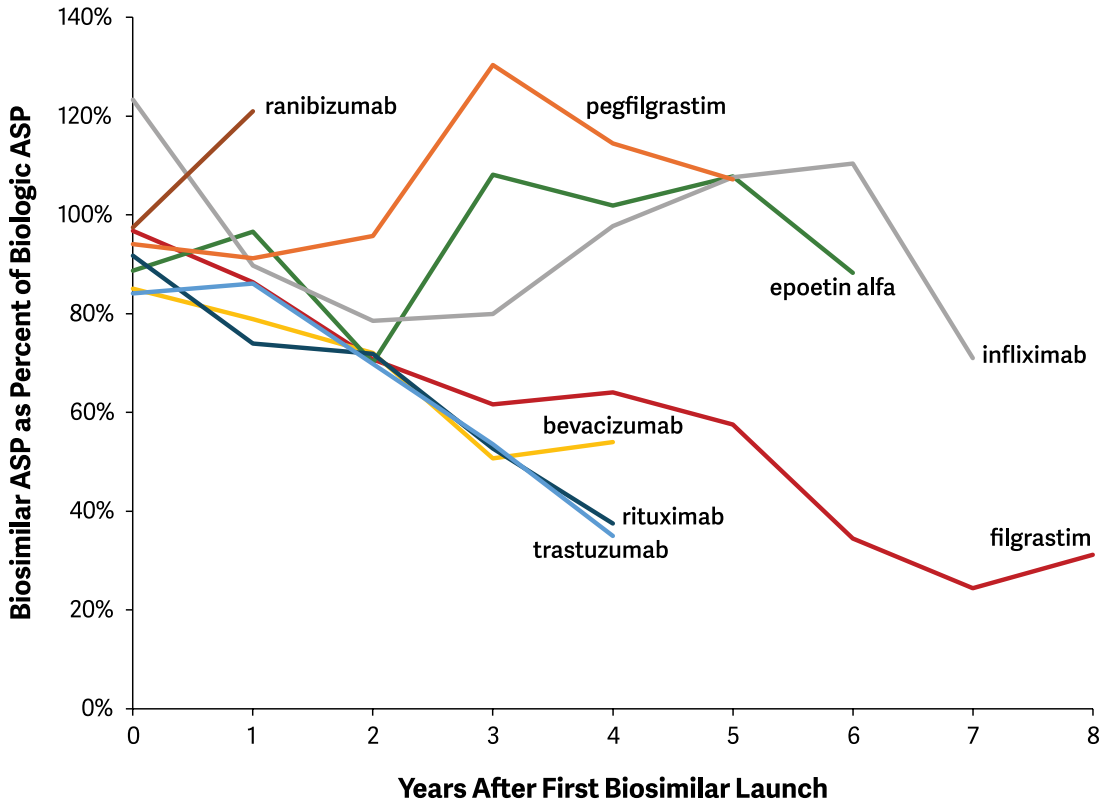
Figure 2: Biosimilar price post-market entry relative to initial originator biologic price[17]



Price discounts offered by biosimilars are realized at differing rates

Additionally, certain originator biologics (e.g., Neulasta [pegfilgrastim]) have adopted more aggressive pricing strategies with biosimilars following their entry, as shown in **Figure 3** which accounts for how biosimilars' and originator biologics' prices change following the entry of biosimilars. Others, however, do not – for example, Neupogen's (filgrastim's) price has stayed relatively constant since biosimilar entry. This further highlights the variation across molecules in terms of biologic and biosimilar pricing following biosimilar market entry.

Figure 3: Biosimilar price post-market entry relative to originator biologic price[18]



Originator biologics compete differently on price with biosimilars

Published literature has assessed the potential drivers of the variation in biologic and biosimilar pricing across molecules. Such potential drivers may include (but are not limited to) differences across products in terms of reimbursements (e.g., originator biologic cost relative to biosimilar cost may differ across payers) and discounts or rebates (e.g., branded biosimilars tend to be offered at smaller discounts but with larger rebates, while unbranded biosimilars tend to be offered at larger discounts).[19] As **Figure 3** demonstrates, pricing strategies taken by biologic manufacturers vary by product. Yet even for originator biologics that do not compete directly on gross price, there are other mechanisms, such as rebates and other discounts, that allow them to compete on net price, and gross price data such as ASP do not reflect these. Given the importance that prices have on competition, these factors become critical to assessing the competitive environment for biologics and biosimilars.

Takeaways regarding uptake and price following biosimilar market entry

The data analyzed in this study show that the uptake and price experience of currently available biologics and biosimilars is varied and not uniform. As a result, in antitrust and competition matters involving biologics and biosimilars, the assumptions relied upon should be tailored to the specific product(s) of interest, and the factors that might be relevant for that set of products must be accounted for specifically. Additionally,

this research stresses the importance of considering a range of different potential drivers when assessing uptake and price trends. As there are only a limited number of molecules for which biosimilars have launched in the U.S., further analyses of uptake and price will be important to identify trends and potential patterns that may emerge.

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Endnotes

1 *See, e.g.*, Henry Grabowski, Genia Long, Richard Mortimer, and Mehmet Bilginsoy, *Continuing trends in U.S. brand-name and generic drug competition*, Journal of Medical Economics (2021), Vol. 24, No. 1, pp. 908-917.

2 IQVIA, *Biosimilars in the United States 2023-2027* (January 2023), available at https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/biosimilars-in-the-united-states-2023-2027, Exhibit 2: 2021 biologics market segmented by status of biosimilar competition and biosimilar development (also see Exhibit 1).

3 *See, e.g.*, Cardinal Health, *Biosimilar Landscape* (May 8, 2024), available at https://www.cardinalhealth.com/content/dam/corp/web/documents/Report/cardinal-health-biosimilar-launches.pdf; Novartis, *FDA approves first biosimilar Zarxio™* (filgrastim-sndz) from Sandoz (March 6, 2016), available at https://www.novartis.com/news/media-releases/fda-approves-first-biosimilar-zarxiotm-filgrastim-sndz-from-sandoz.

4 IQVIA, *Biosimilars in the United States 2023-2027* (January 2023), available at https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/biosimilars-in-the-united-states-2023-2027, Exhibit 2: 2021 biologics market segmented by status of biosimilar competition and biosimilar development (also see Exhibit 1). Of the $260 billion spent on biologics in the U.S. in 2021: (i) $38 billion (14 percent) was spent on biologics facing biosimilar competition; (ii) $181 billion (70 percent) was spent on biologics that may face future biosimilar competition; and (iii) $41 billion (16 percent) was spent on non-recombinant/vaccine biologics.

5 IQVIA, *Biosimilars in the United States 2023-2027* (January 2023), available at https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/biosimilars-in-the-united-states-2023-2027, Exhibit 2: 2021 biologics market segmented by status of biosimilar competition and biosimilar development (also see Exhibit 1). Of the remaining $181 billion spent on biologics that may face future biosimilar competition, $86 billion was spent on biologics for which biosimilars were not yet in development as of 2021.

6 *CareFirst of Maryland, Inc., et al. v. Johnson & Johnson and Janssen Biotech Inc.*, 2:23-cv-00629-JKW-LRL, United States District Court for the Eastern District of Virginia Norfolk Division (December 7, 2023); *Mylan Pharmaceuticals Inc., et al. v. Sanofi-Aventis U.S. LLC, et al.*, 2:23-cv-00836-MRH, United States District Court for the Western District of Pennsylvania (November 20, 2023).

7 Christopher T. Holding and Kevin J. DeJong, *The Seventh Circuit Affirms Dismissal of the HUMIRA Antitrust Litigation, Big Molecule Watch* (August 3, 2022), available at https://www.goodwinlaw.com/en/insights/blogs/2022/08/the-seventh-circuit-affirms-dismissal-of-the-humir.

8 FDA and Federal Trade Commission, *Joint Statement of the Food & Drug Administration and the Federal Trade Commission Regarding a Collaboration to Advance Competition in the Biologic Marketplace* (February 3, 2020), available at https://www.fda.gov/media/134864/download.

9 Cardinal Health, *2023 Biosimilars Report* (January 2023), available at https://www.cardinalhealth.com/content/dam/corp/web/documents/Report/cardinal-health-biosimilars-report-2023.pdf, Figure 3: Adoption speed (as of Sept. 2022). The analysis uses IQVIA National Sales Perspectives (NSP) data which measure dollar and unit sales for pharmaceutical products across multiple distribution channels, including retail, mail, and non-retail. *See* IQVIA, *Available IQVIA Data*, available at https://www.iqvia.com/insights/the-iqvia-institute/available-iqvia-data. Inflectra launched in November 2016 as the first biosimilar to the infliximab originator biologic, Remicade. *See* Pfizer, *Pfizer Announces the U.S. Availability of Biosimilar Inflectra® (infliximab-dyyb)* (October 17, 2016), available at https://www.pfizer.com/news/press-release/press-release-detail/pfizer_announces_the_u_s_availability_of_biosimilar_inflectra_infliximab_dyyb.

10 Cardinal Health, *2023 Biosimilars Report* (January 2023), available at https://www.cardinalhealth.com/content/dam/corp/web/documents/Report/cardinal-health-biosimilars-report-2023.pdf, Figure 3: Adoption speed (as of Sept. 2022). Mvasi launched in July 2019 as the first biosimilar to the bevacizumab originator biologic, Avastin. *See* Ran Jin, Reshma L. Mahtani, Neil Accortt, Tatiana Lawrence, Darcie Sandschafer, and Arturo Loaiza-Bonilla, *Clinical and treatment characteristics of patients treated with the first therapeutic oncology biosimilars bevacizumab-awwb and trastuzumab-anns in the US,* Therapeutic Advances in Medical Oncology (August 2021), Vol. 13, pp. 1-15. Figure 3 of the Cardinal Health Biosimilars Report indicates that filgrastim had the highest biosimilar uptake among the molecule families represented. This reported uptake for filgrastim includes Granix as a filgrastim biosimilar, as indicated by Figure 1 of the Cardinal Health Biosimilars Report. Granix was approved through a biologics license pathway prior to the adoption of the Biologics Price Competition and Innovation Act (BPCIA) of 2009. As a result, other or future analyses of biosimilar uptake may not include Granix as a filgrastim biosimilar. *See, e.g.*, Alice J. Chen, Rocia Ribero, and Karen Van Nuys, P*rovider Differences in Biosimilar Uptake in the Filgrastim Market*, The American Journal of Managed Care (May 2020), Vol. 25, No. 5, pp. 208–213.

11 Such characterizations of generic uptake only represent the "average" experience, and do not represent the wide range of potential outcomes associated with generic entry. *See, e.g.*, Benjamin N. Rome, ChangWon C. Lee, Joshua J. Gagne, and Aaron S. Kesselheim, *Factors Associated With Generic Drug Uptake in the United States, 2012 to 2017*, Health Policy Analysis (2021), Vol. 24, No. 6, pp. 804–811, at 810 ("We found that generic uptake after brand-name drugs lose market exclusivity is highly variable.")

12 "Biosimilar Uptake Share" estimated based on analysis of IQVIA NSP data included in Figure 3: Adoption speed (as of Sept. 2022) of Cardinal Health's 2023 Biosimilars Report. *See* Cardinal Health, *2023 Biosimilars Report* (January 2023), available at https://www.cardinalhealth.com/content/dam/corp/web/documents/Report/cardinal-health-biosimilars-report-2023.pdf; "Average generic small-molecule drugs" estimated for the first twelve months based on average generic uptake between 2017–2019 per Grabowski, et al. (2021), with the series projected beyond twelve months based on the assumption that a 90 percent generic share is ultimately achieved. See Henry Grabowski, Genia Long, Richard Mortimer, and Mehmet Bilginsoy, *Continuing trends in U.S. brand-name and generic drug competition*, Journal of Medical Economics (2021), Vol. 24, No. 1, pp. 908–917; KPMG, Generics 2030: Three strategies to curb the downward spiral (2020), available at https://kpmg.com/kpmg-us/content/dam/kpmg/pdf/2023/generics-2030.pdf; Ernst R. Berndt, Richard Mortimer, Ashoke Bhattacharjya, Andrew Parece, and Edward Tuttle, *Authorized Generic Drugs, Price Competition, and Consumers' Welfare*, Health Affairs (2007), Vol. 26, No. 3, pp. 790–799.

13 *See, e.g.*, Hillel Cohen, Donna Beydoun, David Chien, Tracy Lessor, Dorothy McCabe, Michael Muenzberg, Robert Popovian, and Jonathan Uy, *Awareness, Knowledge, and Perceptions of Biosimilars Among Specialty Physicians*, Advanced Therapeutics (2016), Vol. 33, No. 12, pp. 2160–2172, at 2160–2161; Jason Chen, Dat Ngo, and Annie Yi, *Biosimilar Impact on Oncology Clinical Trial Design and Operations*, JCO Oncology Practice (2021), Vol. 18, No. 3, pp. 157–161.

14 Richard G. Frank, Thomas G. McGuire, and Ian Nason, *The Evolution of Supply and Demand in Markets for Generic Drugs*, The Milbank Quarterly (2021), Vol. 99, No. 3, pp. 828–852.

15 Richard G. Frank, Mahnum Shahzad, Aaron S. Kesselheim, and William Feldman, *Biosimilar competition: Early learning*, Health Economics (January 12, 2022), Vol. 31, pp. 647–663.

16 IMS Institute for Healthcare Informatics, *Price Declines after Branded Medicines Lose Exclusivity in the U.S.* (January 2016), available at https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/price-declines-after-branded-medicines-lose-exclusivity-in-the-us.pdf.

17 Prices for biosimilars and originator biologics are estimated using CMS Medicare Part B ASP data. Biosimilar price share is calculated by dividing the average of all biosimilar ASPs in each quarter by the originator biologic ASP in the quarter immediately preceding the launch of the first biosimilar. "Average generic small-molecule drugs" are estimated as average generic oral small-molecule drug prices as a share of their reference brand product prices. *See* IMS Institute for Healthcare Informatics, *Price Declines after Branded Medicines Lose Exclusivity in the U.S.* (January 2016), available at https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/price-declines-after-branded-medicines-lose-exclusivity-in-the-us.pdf.

18 Prices for biosimilars and originator biologics are estimated using CMS Medicare Part B ASP data. Biosimilar price share is calculated by dividing the average of all biosimilar ASPs by the contemporaneous originator biologic ASP in each quarter.

19 *See, e.g.*, Pinar Karaca-Mandic, Jessica Chang, Ronald Go, Stephen Schondelmeyer, Daniel Weisdorf, and Molly Moore Jeffery, *Biosimilar Filgrastim Uptake And Costs Among Commercially Insured*, Medicare Advantage, Health Affairs (November 2019), Vol. 38, No. 11, pp. 1887–1892; Skylar Jeremias and Ashley Gallagher, *Why Are Companies Launching Biosimilars With 2 Prices?* Julie Reed Explains, The Center for Biosimilars (July 30, 2023), available at https://www.centerforbiosimilars.com/view/why-are-companies-launching-biosimilars-with-2-prices-julie-reed-explains; Mariam E. Sunny and Patrick Wingrove, *Boehringer launches 81% discounted biosimilar of AbbVie's Humira*, Reuters (October 3, 2023), available at https://www.reuters.com/business/healthcare-pharmaceuticals/boehringer-launches-unbranded-humira-biosimilar-81-discount-2023-10-02/.