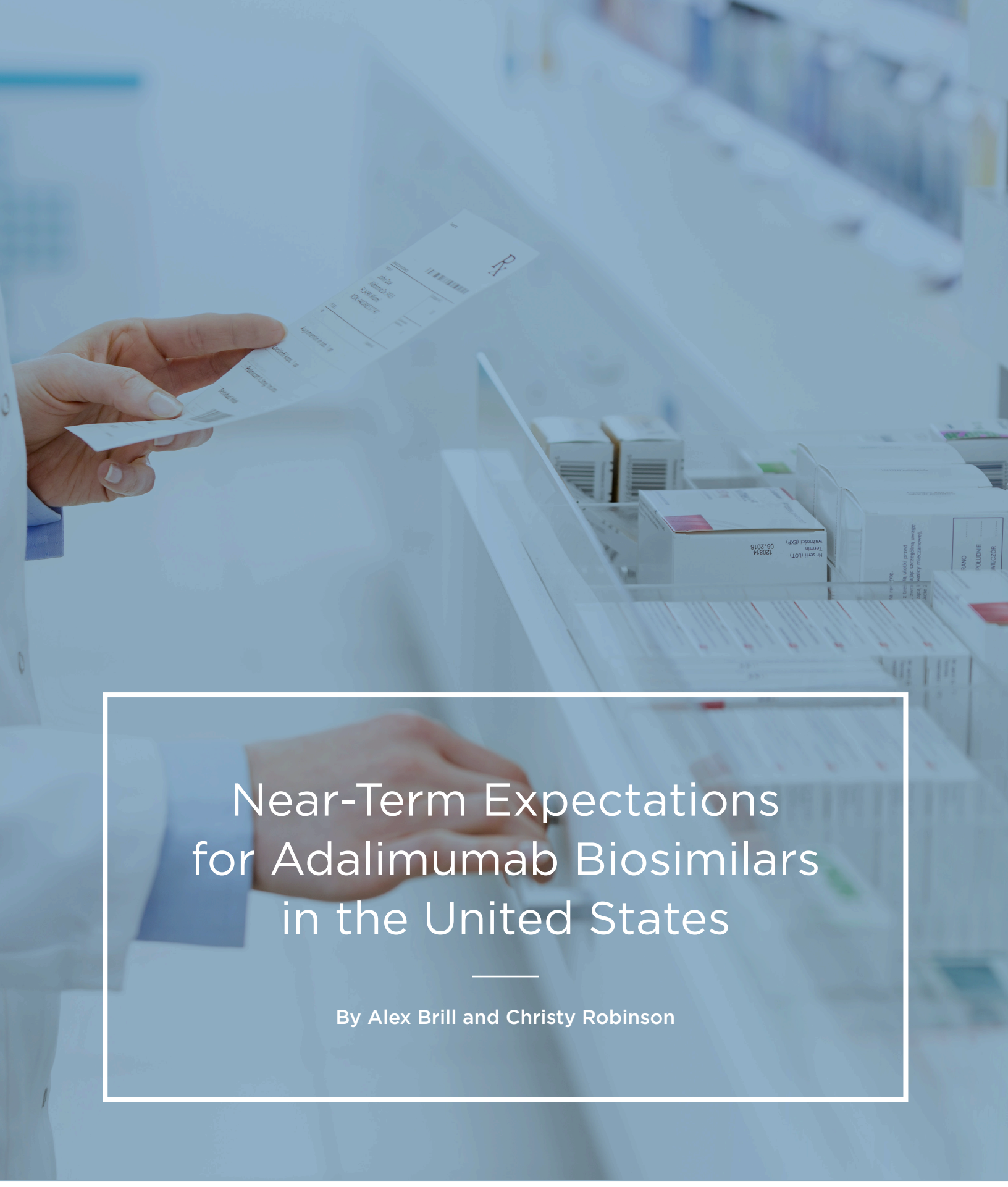

Near-Term Expectations for Adalimumab Biosimilars in the United States

By Alex Brill and Christy Robinson

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Overview

Humira (adalimumab) has led the US prescription-drug market in sales for years, but its monopoly has come to an end. The first US adalimumab biosimilar, Amgen's Amjevita, launched on January 31, 2023. Over the remainder of the year, as many as eight more biosimilars are set to enter the US market, where AbbVie, the reference product manufacturer, derives more than 87 percent of its global Humira revenues (*AbbVie, 2023*). This paper explores this long-awaited moment and the expected transition from a monopolistic adalimumab market to a competitive marketplace with multiple biosimilars.

Humira's worldwide sales total $200 billion, making it the highest-selling drug of all time (*Wainer, 2021*). In total, more than 1.4 million patients have been prescribed Humira (*AbbVie, 2022*). In the United States, more than 300,000 patients were prescribed the blockbuster drug in 2020 alone (*ClinCalc, 2021*). Unsurprisingly, Humira already has more biosimilar competitors approved by the US Food and Drug Administration (FDA) than any other reference biologic. However, only Amjevita is currently on the market. The next biosimilars to launch will not do so until July 2023.

However, while 2023 marks an important turning point for patients who rely on adalimumab, the evolution from a Humira monopoly to robust competition will take time. As this paper explains, we expect a lengthier transition than we have seen with other biologic drugs.

The paper is organized as follows. **Section 1** provides an overview of Humira, including its market size, indications, and key aspects of its significance in the marketplace, as well as adalimumab biosimilars anticipated in 2023. **Section 2** reviews pricing and utilization trends from launches of biosimilars for other brand products. **Section 3** discusses expected trends in the adalimumab market and highlights challenges in observing cost savings attributable to adalimumab biosimilars.

Key Points

- Biosimilar competition for Humira (adalimumab), the top-selling drug in the United States, has finally arrived.
- The launch of biosimilar adalimumab also represents the introduction of biosimilars to the pharmacy-benefit market, which has distinctly different dynamics from the medical-benefit market.
- Potential cost savings from adalimumab biosimilars are significant. But a competitive market will take time to mature, and savings will be slower to accrue than has been the case for existing, provider-administered biosimilars.

1. The Adalimumab Market

Humira is a tumor necrosis factor (TNF) blocker used to treat anti-inflammatory conditions and autoimmune diseases. The drug was first approved by the FDA for severe rheumatoid arthritis in 2002 and has since received approvals for juvenile idiopathic and psoriatic arthritis, Crohn's disease, ulcerative colitis, and plaque psoriasis, among other conditions. In 2003, Humira was approved in 38 additional countries.

A single-use, disposable, self-injectable Humira pen, which enhanced convenience for patients, received FDA approval in 2006. In 2018, the FDA approved Humira citrate-free, a new formulation that lessens the discomfort or pain associated with injection for some patients. The majority of Humira patients now use the citrate-free version.

AbbVie has been criticized for excessive price increases for Humira over the years. . . . From 2009 to 2018, Humira's net price increased by 110 percent.

Humira is primarily dispensed through retail pharmacies and is covered under Medicare Part D or the pharmacy benefit of commercial insurance plans. In the United States, most biologic — and, until adalimumab biosimilars, all non-insulin biosimilars — are administered by a licensed provider in a healthcare setting and covered under Medicare Part B or the medical benefit of commercial plans. As one expert recently explained, with Part B or medical-benefit drugs, "large health systems have relative control. They can . . . build system-preferred biosimilars in their electronic health record system in ways that guide physicians to prescribe the health system–preferred biosimilars" (*Humphreys, 2023*). The dynamics in Part D and commercial pharmacy benefits are different, with more decision-making at the provider and patient level and greater significance of formularies, which govern coverage of different products.

Humira has been a record-setting money maker for AbbVie. After decades of steady growth, worldwide sales of the drug exceeded $21 billion in 2022 (*AbbVie, 2023*). The revenue is not all volume driven. AbbVie has been criticized for excessive price increases for Humira over the years. For example, a staff report from the US House of Representatives Committee on Oversight and Reform (*2021*) found that from 2009 to 2018, Humira's net price increased by 110 percent.

ADALIMUMAB BIOSIMILARS

The adalimumab biosimilars set to launch in the United States in 2023 are expected to come in three waves. As mentioned above, Amgen's Amjevita entered the market on January 31, 2023. Additional biosimilars, including Boehringer Ingelheim's Cyltezo, Coherus BioSciences's Yusimry, Fresenius Kabi's Idacio, Biocon's Hulio, and Samsung Bioepis/Organon's Hadlima and Hadlima HC, are expected to enter in or around July 2023. In fall 2023, Pfizer's Abrilada and Sandoz's Hyrimoz are expected to launch. In addition to these nine, for which the FDA has

already granted approval, Alvotech/Teva and Celltrion may launch their adalimumab biosimilars in July if they are approved by that time. (See **Table 1** and **Table 2** for details on adalimumab biosimilars approved by the FDA and pending approval, respectively.)

While each approved biosimilar has been shown to have the same clinical efficacy as the reference product, adalimumab biosimilars may differ in concentration, use of citrate, and interchangeability designation. As explained in the next section, these differences have ramifications for the evolution of the adalimumab market.

TABLE 1. FDA-Approved Adalimumab Biosimilars

BIOSIMILAR NAME (MANUFACTURER)	Approval Date	Concentration	Citrate-Free	Interchangeable	Anticipated Launch
Amjevita (Amgen)	9/23/2016	Low	Yes	No	Launched January 2023
Cyltezo (Boehringer Ingelheim)	8/25/2017	Low	Yes	Yes	July 2023
Yusimry (Coherus BioSciences)	12/17/2021	Low	Yes	No	July 2023
Idacio (Fresenius Kabi)	12/13/2022	Low	Yes	No	July 2023
Hulio (Biocon)	7/6/2020	Low	Yes	No	July 2023
Abrilada (Pfizer)	11/15/2019	Low	Yes	Pending	November 2023
Hadlima (Samsung Bioepis/ Organon)	7/23/2019	Low	No	Pending	July 2023
Hadlima HC (Samsung Bioepis/ Organon)	8/15/2022	High	Yes	Pending	July 2023
Hyrimoz (Sandoz)	10/30/2018	Low	No	No	July 2023

Source: *Cardinal Health (2023), Goodroot (2023), and Martin (2022).*

TABLE 2. Adalimumab Biosimilars Pending FDA Approval

BIOSIMILAR NAME (MANUFACTURER)	Concentration	Citrate-Free	Interchangeable	Anticipated Launch
Amjevita HC (Amgen)	High	Yes	Pending	TBD
Hyrimoz HCF (Sandoz)	High	Yes	Unknown	July 2023
Yusimry HC (Coherus BioSciences)	High	Unknown	Unknown	Unknown
Yuflyma (CT-P17) (Celltrion)	High	Yes	Pending	July 2023
AVT02 (Alvotech/Teva)	High	Yes	Pending	July 2023

Source: *Cardinal Health (2023), Goodroot (2023), and Martin (2022).*

2. Biosimilar Price and Utilization Trends

The question on everyone's mind as adalimumab biosimilars enter the US market is how much savings they will generate. With 2022 US sales of Humira topping $18.6 billion (*AbbVie, 2023*), the savings potential from adalimumab biosimilars is enormous. But savings are a function of price and utilization, both of which are yet to be determined for adalimumab products. While we expect some important differences in the evolution of the adalimumab market (detailed below), pricing and utilization trends observed in other US biosimilar markets and the European adalimumab market can be informative in the absence of adalimumab data.

In Europe, adalimumab biosimilars launched in 2018 with 18–40 percent price discounts (*Coghlan et al., 2021*). In the first year, biosimilars captured 35 percent of the European adalimumab market, though data vary by country (*ibid.*). There are now 10 adalimumab biosimilars available in Europe (*IQVIA, 2022a*).

In the United States, 26 biosimilars are on the market, competing with 12 reference biologics (*Center for Biosimilars, 2023*). In 2021, savings to the US healthcare system attributable to biosimilars totaled $7 billion (*AAM, 2022*). Depending on the disease area, US biosimilars launch at a 10–57 percent price discount from the pre-biosimilar reference product price and achieve 32–82 percent market share (*Amgen, 2022*).

Particularly noteworthy is that reference product prices typically decline when biosimilars are on the market. In a recent analysis, we looked at biologics covered under the medical benefit of commercial insurance plans in three disease areas. Our results showed that both biosimilar and reference biologic prices declined over time, and prices declined more rapidly for biosimilars than for reference biologics in two of the three disease areas (*Brill and Robinson, 2022*).

Looking at molecules with biosimilars available in the United States, IQVIA (*2023*) shows that costs for reference products and biosimilars have declined 18–50 percent per unit since biosimilar entry.

Also noteworthy is that price declines occurred over three to four years in our analysis. Amgen (*2022*) illustrates that biosimilar prices in the initial year of launch are generally only modestly discounted relative to their reference product. Likewise, IQVIA (*2023*) finds that recently launched biosimilars have gained substantial market share, but over several years. In other words, trends observed in other biosimilar markets show that price declines and uptake take time. For reasons explained below, we anticipate the evolution of the adalimumab market to be even slower.

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3. Expected Adalimumab Trends

As the first non-insulin biosimilar in the pharmacy benefit, adalimumab is in uncharted territory. Unlike the medical benefit, the pharmacy benefit is characterized by negotiations between drug manufacturers and pharmacy benefit managers (acting on behalf of payers). In these negotiations, rebates can drive formulary placement — and thus utilization — of drugs. Rebates also mean that net prices are not readily observable.

ADALIMUMAB FORMULARY PLACEMENT

In the near term, the major pharmacy benefit managers have announced that Humira will remain on formulary at parity with covered adalimumab biosimilars. AbbVie's CEO recently noted that the company has "secured Humira formulary access for more than 90% of the US covered lives this year" (*J.P. Morgan, 2023*). This means that patients will have no incentive to use a biosimilar over Humira, and utilization management strategies — for example, prior authorization and step therapy — will not preference the biosimilar.

Over time, as patients, prescribers, and payers gain experience with adalimumab biosimilars and prices fall, formulary placement is likely to improve for covered biosimilars relative to Humira. We document this trend for biosimilars in the medical benefit (*Brill and Robinson, 2022*).

ADALIMUMAB UTILIZATION

In addition to formulary placement, uptake of biosimilar adalimumab will be slow for several other reasons. First, Amjevita, the newly launched adalimumab biosimilar, is a low-concentration version and only directly competes with approximately 15 percent of the current Humira market (*Goodroot, 2023*). Multiple high-concentration biosimilar applications are pending approval by the FDA, but only one high-concentration biosimilar (Samsung Bioepis/Organon's Hadlima HC) has received FDA approval and will not launch until July 2023.

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Second, AbbVie has a significant market advantage over biosimilar competitors and can leverage relationships with payers to hinder biosimilar uptake. At the very least, existing multiyear contracts for Humira will slow biosimilar adoption.

Third, only one approved adalimumab biosimilar (Boehringer Ingelheim's Cyltezo) is interchangeable with Humira. In the pharmacy benefit, generic utilization skyrockets upon generic entry because of automatic substitution policies. But adalimumab biosimilars cannot be subject to these policies if they are not interchangeable. It remains uncertain when additional adalimumab biosimilars will receive an interchangeable designation.

Finally, adalimumab treats chronic diseases, with patients often remaining on the drug for years. The number of new starts — those likely to be prescribed a biosimilar — is only a fraction of total patients.

Amgen's Murdo Gordon recently noted that, as "the first significant US biosimilar in the pharmacy benefit space, we expect gradual uptake in the coming months as this market evolves" (*Wallace, 2023a*). J.P. Morgan analysts predict that AbbVie will maintain approximately 90 percent market share in 2023 but provide "increased price concessions, particularly in the second half of 2023 as more suppliers enter the market" (*Wallace, 2023b*).

ADALIMUMAB PRICES

Robust competition is needed to drive down prices, and biosimilar competitors need time to achieve stable, sustainable prices consistent with market demand. As IQVIA (*2023*) notes, "In the future, especially in medicines with larger spending, pricing impacts may still be driven by third-or-later entrants, as they may seek more aggressive contracting and discounting."

When multiple adalimumab biosimilars launch this summer, they may drive steeper price discounts than during the first half of the year. However, this process, where manufacturers iterate with payers over time and prices evolve, may be more complex for adalimumab given the large number of biosimilars and staggered launch dates. Goodroot (*2023*) estimates that "downward pressure on [adalimumab] drug cost will be minimal, at least initially."

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Additionally, manufacturer rebates will make list prices relatively uninformative. For example, Amgen launched Amjevita with two list prices — 5 and 55 percent below Humira's list price — and acknowledged that rebates would drive actual prices (*Wallace, 2023b*). As health policy scholars have noted, "The potential market for the low list price version will be constrained to the modest portion of the market which does not prioritize rebates. This likely includes some integrated health systems like Kaiser which effectively act as both the insurer and provider" (*Gottlieb and Ippolito, 2023*).

The lack of publicly observable net prices for pharmacy-benefit drugs complicates the ability for policymakers and the public to observe the savings achieved by adalimumab biosimilars.

This pricing structure mimics the strategy used by the manufacturer of the insulin biosimilar Semglee in the pharmacy benefit (*Becker, 2023*). For Semglee, the version with the low list price has seen greater uptake in Medicaid, while the high-list-price version has higher market share among commercial payers (*IQVIA, 2022b*).

CHALLENGES IN OBSERVING ADALIMUMAB BIOSIMILAR PRICES

The lack of publicly observable net prices for pharmacy-benefit drugs complicates the ability for policymakers and the public to observe the savings achieved by adalimumab biosimilars. For medical-benefit drugs, Part B average sales prices are public (albeit with a two-quarter lag), making it possible to easily calculate biosimilar savings.

Stakeholders have grown accustomed to having access to average net prices for biosimilars, but in the pharmacy benefit, only list prices are publicly available. While some information may be revealed in manufacturers' public financial reporting, the lack of actual net price data for adalimumab biosimilars may cloud perceptions about savings.

Additionally, for biosimilar manufacturers who are working to strategically price products to both gain market share and recoup development costs, the lack of publicly available price data for competitors creates additional challenges.

In short, we expect significant adalimumab savings to take several years to develop. But we also expect these savings to be more difficult to observe than savings in the medical benefit.

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Conclusion

Adalimumab biosimilars will achieve substantial savings, but stakeholders should recognize that 2023 will be just the beginning of a transition to a competitive market. As this paper demonstrates, the transition to robust competition for adalimumab will be gradual, reflecting the specific nature of the market for pharmacy-benefit prescription drugs, payers' formulary decisions, and particular clinical aspects of the products. Savings will accrue to Medicare, Medicaid, and commercial payers as competition leads to lower net prices for adalimumab, but full savings will be realized only after utilization of adalimumab biosimilars becomes significant and price discounts fully materialize.

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ABOUT THE AUTHORS

Alex Brill is the founder and CEO of Matrix Global Advisors (MGA), an economic policy consulting firm. He previously served on the staff of the House Ways and Means Committee and the White House Council of Economic Advisers.

Christy Robinson is a principal at MGA.

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