EXHIBIT A

UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF PENNSYLVANIA

PFIZER, INC., *Plaintiffs,* –v– JOHNSON & JOHNSON and JANSSEN BIOTECH, INC. *Defendants.*	**Civil Action No. 2:17-cv-04180-JCJ**

[PROPOSED] BRIEF OF THE BIOSIMILARS COUNCIL AS *AMICUS CURIAE* IN OPPOSITION TO DEFENDANTS' MOTION TO DISMISS

TABLE OF CONTENTS

TABLE OF AUTHORITIES

CASES

STATUTES AND PUBLIC LAWS

OTHER AUTHORITIES

STATEMENT OF INTEREST OF *AMICUS CURIAE*

Proposed *amicus curiae* the Biosimilars Council respectfully submits this brief in opposition to Defendants' Johnson & Johnson ("J&J") and Janssen Biotech, Inc.'s ("Defendants") motion to dismiss the complaint ("Compl.") brought by Plaintiff Pfizer, Inc. ("Pfizer").[1]

The Biosimilars Council is a division of the Association for Accessible Medicines ("AAM"), the non-profit voluntary trade association representing companies that develop and manufacture generic and biosimilar medicines reviewed and approved by the Food and Drug Administration ("FDA"). AAM represents nearly 100 manufacturers and distributors of finished generic pharmaceutical products, manufacturers and distributors of bulk active pharmaceutical ingredients, and suppliers of other goods and services to the generic pharmaceutical industry. AAM's members provide Americans with generic and biosimilar medicines that are as safe and effective as their brand-name counterparts, but are substantially more affordable, accounting for roughly 89% of all prescriptions dispensed in the United States but only 26% of total spending on prescriptions.

The Biosimilars Council's members include companies working to develop biosimilar products for the United States pharmaceutical market.[2] The Biosimilars Council frequently participates as an *amicus curiae* in cases involving the regulation and availability to patients of biosimilars.

Biosimilars are highly similar versions of FDA-licensed branded biologic medicines. A branded biologic in this context is known as a "reference product" or "reference listed drug"

---

[1] A motion for leave to submit this *amicus* brief is being filed contemporaneously herewith. Plaintiff has consented to the filing of the *amicus* brief, and Defendants do not oppose the filing of the brief.

[2] Pfizer is not a member of the Biosimilars Council.

("RLD") and its licenseholder as the "Reference Product Sponsor" ("RPS").[3] Congress established an expedited FDA approval pathway for biosimilars in 2010 in the Biologics Price Competition and Innovation Act ("BPCIA").[4] A principal goal of the BPCIA was to encourage competition in markets for biologics, which are among the most expensive pharmaceutical products on the market today. The BPCIA regime is analogous to (though in important ways different from) the regime for expedited approval of small molecule generic drugs Congress created over 30 years ago when it passed the Hatch-Waxman amendments to the Federal Food, Drug and Cosmetic Act (the Drug Price Competition and Patent Term Restoration Act of 1984, Pub. Law No. 98-417, 98 Stat. 1585 (1984)). Hatch-Waxman has saved the health care system $1.67 trillion over the last decade. Association for Accessible Medicines, *Generic Drug Access and Savings in the U.S.* (2017), at 20.

This case presents critical issues regarding the degree to which biosimilars — and the still nascent industry focused on affordable biologic medicines — will be allowed to compete on fair terms with higher-priced branded biologic medicines, as Congress intended when it enacted the BPCIA. The biosimilar at issue in this case − Pfizer's Inflectra® (infliximab) − is one of only a handful of biosimilars that has been approved by FDA under the BPCIA, but many more are in active development. As more biosimilars are approved, however, exclusionary tactics such as those used by Defendants to prevent Inflectra from competing against Defendants' branded infliximab product Remicade®, if upheld, will provide a roadmap for other pharmaceutical companies to stifle biosimilar competition. Replication of these tactics across biologics markets will dramatically diminish incentives for developing future biosimilars, and competition in this

[3] Reference products are licensed under section 351(a) of the Public Health Services Act ("PHSA"), 42 U.S.C. § 262(a). The expedited biosimilars pathway was added by the Biologics Price Competition and Innovation Act to the PHSA as section 351(k), 42 U.S.C. § 262(k).

[4] Pub. L. No. 111-148, §§ 7001 *et seq.*, 124 Stat. 119, 804 (2010).

critical, growing sector of the health care industry will suffer. In short, this case will help define the scope of antitrust protections for biosimilars for years to come and determine the viability of the industry that Congress sought to create through the BPCIA. Thus, the Biosimilars Council and its members have a strong interest in this case that goes beyond the specific dispute between Pfizer and the Defendants over infliximab products.

SUMMARY

Pfizer addressed in its opposition to Defendants' motion to dismiss ("Pfizer Mem. Opp'n") why that motion should be denied, and *amicus* will not repeat those arguments here. Rather, this brief seeks to support Pfizer's position by providing important context showing the critical need for robust competition in biosimilars markets, the great potential of the biosimilars industry to achieve massive savings for the U.S. healthcare system, and the threat posed to that industry as a whole by the kinds of exclusionary conduct engaged in by Defendants in this case.

BACKGROUND

A. There is a critical need for competition in the market for prescription biologic drugs.

Biosimilars are expected to be one key factor in efforts to contain prescription drug costs. Biologics, unlike the relatively simple small-molecule drugs covered under Hatch-Waxman, are complex, large-molecule medicines derived from living organisms and are used to treat a range of serious conditions, including rheumatoid arthritis, plaque psoriasis, Crohn's disease, lymphoma, leukemia, breast cancer, and diabetes – some of which are treated by the infliximab products at issue in this case. Biologics are among the most expensive prescription drugs in the United States and account for an increasing share of U.S. prescription drug costs. Federal Trade Comm'n, Public Workshop: Follow-On Biologics: Impact of Recent Legislative and Regulatory Naming Proposal on Competition, 78 Fed. Reg. 68,840 (Nov. 15, 2013) (noting that biologics are

"among the most important pharmaceutical products in the United States" and "comprise the fastest growing sector within pharmaceuticals."). *See also* Biosimilars Council, *Biosimilars in the United States: Providing More Patients Greater Access to Lifesaving Medicines* (2017) ("Biosimilars Council")[5] at 2 (noting that biologic sales have increased 65% since 2011, reaching more than $105 billion in 2016, and citing QuintilesIMS, *Medicines Use and Spending in the U.S. A Review of 2016 and Outlook to 2021* (Apr. 2017)); Dep't of Health and Human Servs., Office of the Assistant Secretary for Planning and Evaluation, *Observations on Trends in Prescription Drug Spending* 3, Table 1 (Mar. 8, 2016) ("2016 ASPE Report")[6] at 8 (noting that spending on specialty drugs (which include biologics) as a percentage of spending on all retail drugs increased from 5.7 percent to 7.6 percent – a 33.3 percent increase – between 2009-2014).

On average, biologics cost $45 per day, compared to $2 per day for small-molecule drugs. Steve Pociask, *NewConsumerGram: Lifesaving Drugs at Lower Costs*, Am. Consumer Inst. Ctr. for Citizen Research 2 (July 22, 2014).[7] Some biologics cost tens or even hundreds of thousands of dollars per patient per year. Many of the top-selling drugs in the world are biologics, including the RLD at issue in this case, Remicade, which generated nearly $5 billion in U.S. sales alone in 2016. Pfizer Mem. Opp'n 5. Humira® (adalimumab), which treats rheumatoid arthritis and other conditions and is the top selling drug in the world, costs over $50,000 per year. Judith A. Johnson, *FDA Regulation of Follow-On Biologics*, Cong. Research Serv., RL34045, 1 (Apr. 26, 2010). The discounted price of a two-week dose of Humira in 2009 was $630; by 2015, it had more than doubled, to $1,331. Robert Langreth, Michael Keller & Christopher Cannon, *Decoding BigPharma's Secret Drug Pricing Practices*, Bloomberg, June

[5] http://biosimilarscouncil.org/wp-content/uploads/2017/09/Biosimilars-Council-Patient-Access-Study-090917.pdf.

[6] https://aspe.hhs.gov/sites/default/files/pdf/187586/Drugspending.pdf.

[7] http://www.theamericanconsumer.org/2014/07/new-consumergram-lifesaving-drugs-at-lower-costs/.

29, 2016, at 3.[8] In 2014, Medicare Part B spent $1.5 billion for the non-Hodgkins lymphoma biologic Rituxan® (rituximab), an increase of nearly 25 percent since 2010. Ctrs. for Medicare and Medicaid Servs., *Medicare Drug Spending Dashboard* (Dec. 21, 2015) Chart 1b.[9] Remicade, the branded biologic at issue in this case, has been on the market and enjoyed monopoly power with respect of infusion-administered therapies for the ailments it treats for nearly 20 years. Many biologic products have been on the market for a decade or more without any competition. Thus, the need for robust price competition in prescription biologics markets could not be more clear or more urgent to provide patient access to life-saving medicines.

B. Congress sought to promote price competition in biologics markets through the BPCIA.

As noted above and in Pfizer's complaint, the BPCIA established an expedited approval pathway for biologics medicines that are deemed by FDA to be (1) "highly similar to" a previously-approved RLD and (2) without "clinically meaningful differences [from the RLD] in terms of safety, purity and potency." 42 U.S.C. § 262(i)(2). Where these criteria are met, FDA may approve the biosimilar product based on the agency's previous findings of safety and efficacy for the RLD, allowing the biosimilar applicant to forego the full range of expensive clinical studies that are required of new drugs. *See Sandoz Inc. v. Amgen Inc.*, ___ U.S. ___, 137 S. Ct. 1664, 1670 (2017) ("[T]he [biosimilar] applicant may piggyback on the showing made by the manufacturer (sponsor) of a previously licensed biologic (reference product).")

Thus, the abbreviated BPCIA pathway, like the analogous Hatch-Waxman pathway for small-molecule generic drugs, serves the dual purposes of (1) reducing biosimilars' development costs and (2) facilitating quicker FDA review, with the goal of getting more, lower-cost products

[8] https://www.bloomberg.com/graphics/2016-drug-prices/.

[9] http://www.cms.gov/Newsroom/MediaReleaseDatabase/Fact-sheets/2015-Fact-sheets-items/2015-12-21.html.

on the market, and therefore to generate greater savings for the healthcare system and increased patient access to life-saving biologic medicines. As Pfizer's complaint explains, these effects were precisely what Congress intended when it passed the BPCIA. Compl. ¶ 32 (quoting congressional statements regarding the goals of the BPCIA).

The BPCIA did not ignore the need to encourage brand drug companies to create new, innovative products. Thus, in addition to creating the expedited approval pathway, and as a legislative *quid pro quo* for that new pathway, Congress granted the original biologic 12 years of statutory exclusivity. 42 U.S.C. § 262(k)(7)(A) (providing that FDA shall not "ma[k]e effective [its licensing of a biosimilar] until the date that is 12 years after the date on which the reference product was first licensed" by FDA); *Amgen*, 137 S. Ct. at 1670. *See also* Thomas M. Burton, *Biosimilar Drugs Face U.S. Test: FDA Panel Will Decide Whether to Recommend Approval*, Wall St. J., Jan. 6, 2015, at 2 ("The 2010 Affordable Care Act created an abbreviated pathway for biosimilars to enter the U.S. market . . . . *As a tradeoff for the industry, the law gave biologic drugs a 12-year period of exclusivity that protected them from competition from a biosimilar*.") (emphasis added).[10] Of course, by its very terms, this exclusivity blocks competition from biosimilars for 12 years *and no more*. Congress fully intended that once this exclusivity period (along with any patent protection) expires and biosimilars for the particular RLDs are approved, robust, unfettered price competition would follow. The exclusionary commercial practices at issue in this case threaten to extend indefinitely the monopolies of brand name drug companies that develop biologics.

[10] http://www.wsj.com/articles/biosimilar-drugs-face-u-s-test-1420590926.

C. Biosimilars hold the promise of massive savings and increased patient access to life-saving medicines.

Increased competition from biosimilars holds the potential for enormous savings for the U.S. healthcare system, with one study estimating reductions in direct spending on biologics of more than $44 billion from 2014-2024. Andrew Mulcahy, Zach Pretmore & Soren Mattke, *The Cost Savings Potential of Biosimilar Drugs in the United States,* RAND Corp. (2014).[11] In Europe, where biosimilars have been marketed since 2004, projected savings from biosimilars through 2020 for three particular product classes have been estimated between €11.8 and €33.4 billion. Robert Haustein, et al., *Saving money in the European healthcare systems with biosimilars*, 1(3-4) Generics & Biosimilars Initiative J. 120-26 (2012).[12] Other estimates are even more optimistic, with one large pharmacy benefit manager with extensive experience and data on biologics concluding that biosimilar versions of 11 high-priced biologics would save the U.S. healthcare system $250 billion from 2014-2024. Express Scripts, *The $250 Billion Potential of Biosimilars* (Apr. 23, 2013).[13] *See also* Biosimilars Council at 2, n.viii (citing separate report estimating annual savings from biosimilars at $250-$275 billion).

Biosimilars hold the promise not only of additional savings to those currently using branded biologic products, but also of increased access to life-saving medicines for those who currently cannot afford the expensive branded versions of these medicines. One study, for example, estimates that 1.2 million U.S. patients could gain access to biologics by 2025 as the result of biosimilar availability, and that women, seniors and low-income patients stand in particular to gain from this increased access. *Id.* at 3-5 (citing study by Avalere Health).

---

[11] http://www.rand.org/content/dam/rand/pubs/perspectives/PE100/PE127/RAND_PE127.pdf.

[12] http://gabi-journal.net/saving-money-in-the-european-healthcare-systems-with-biosimilars.html.

[13] http://lab.express-scripts.com/lab/insights/industry-updates/the-$250-billion-potential-of-biosimilars.html.

D. There are significant costs associated with developing and marketing biosimilars.

Notwithstanding the abbreviated BPCIA pathway, biosimilars are much more expensive to develop and market than small-molecule generic drugs.

Development. A small-molecule generic drug is essentially a copy of its brand-name RLD. Accordingly, a generic drug applicant must merely demonstrate that its product is therapeutically equivalent to the RLD – *i.e.*, that the generic product has the same active ingredient, dosage form, strength, and route of administration as and is "bioequivalent to" (which typically means that it is absorbed into the blood stream at the same rate as) the RLD. 21 U.S.C. § 355(j)(2)(A)(ii)-(iv). This "sameness" standard is generally met through the use of simple comparative blood level studies that are far less expensive and time-consuming than clinical studies designed to establish a new drug's safety and effectiveness. A small molecule generic drug can generally be developed for approximately $1-4 million. Erwin A. Blackstone and P. Fuhr Joseph, Jr., *The Economics of Biosimilars*, Am. Health Drug Benefits (Sept.-Oct. 2013) ("Blackstone") at 471.[14] By contrast, as discussed above, the standard for approval under the BPCIA is that the biosimilar is "highly similar to" – not the same as – the RLD and that it is without "clinically meaningful differences [from the RLD] in terms of safety, purity and potency." 42 U.S.C. § 262(i)(2).[15] Meeting this standard will in general require at least some clinical study of the biosimilar's effects in humans. While FDA has already approved biosimilar versions of certain less complex biologics, it is in the process of determining and explaining the kinds of clinical studies it will require to prove biosimiliarity for more complex biologic products. *See generally* FDA Guidance for Industry, *Scientific Considerations in Demonstrating*

[14] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4031732.

[15] The "highly similar" standard derives from the difficulty of creating biologic products that are identical to an RLD, given the relative complexity of large molecule biologics created from living organisms as compared to small-molecule drugs that are synthesized in laboratories.

Biosimiliarity to a Reference Product (Apr. 2015).[16] One report estimates the cost of developing a biosimilar at $100-$250 million – significantly less than the typical cost of developing a new drug, but much more than the cost of developing a traditional generic copy. Blackstone at 471.

Marketing. Marketing of small-molecule generic drugs is much less expensive than the marketing of biosimilars. Because traditional generic drugs are simply copies of their RLDs, they are subject to state generic substitution laws that, depending on the state, either permit or require pharmacies to substitute the (less expensive) approved generic version of a product for the (more expensive) RLD. These substitution laws mean that a generic manufacturer does not need to spend significant resources promoting its product. By contrast, biosimilars, which are not the "same as" but merely "highly similar to" their RLDs, are not generally covered by state substitution laws.[17] Therefore, a manufacturer of an approved biosimilar – unlike the seller of an approved traditional generic – will likely expend substantial resources to convince providers and patients to switch from the RLD to its product. *See* Aaron Hakim and Joseph S. Ross, *Obstacles to the Adoption of Biosimilars for Chronic Diseases*, JAMA, vol. 317, no. 21 (June 6, 2017) ("JAMA") (Ex. 1 to this brief), at 2163 (noting that "even without sales and marketing support, lower-priced generics typically gain substantial market share through automatic substitution,"

[16] https://www.fda.gov/downloads/drugs/guidances/ucm291128.pdf.

[17] However, the BPCIA also provides for an FDA determination that a biosimilar is also "interchangeable" with – and therefore substitutable for − the RLD, based on FDA's conclusion that the biosimilar is expected to produce the same clinical result as the RLD in any given patient and, for products administered to a patient more than once, there is no greater risk in terms of safety and reduced efficacy from switching back and forth between an interchangeable product and the RLD than from uninterrupted use of the RLD. 42 U.S.C. §§ 262(i)(3), (k)(4). FDA only published draft interchangeability guidelines in 2017 and has yet to approve an interchangeable biosimilar. However, as noted by FDA Commissioner Scott Gottlieb, the agency has made it is clear that it expects non-interchangeable biosimilars to "potentially reduce costs for consumers by creating price competition for products that previously faced few market competitors." *See* Scott Gottlieb & Leah Christl, FDA Voice, *FDA Taking New Steps to Better Inform Physicians About Biosimilars Through Education about these Potentially Cost-Saving Options* (Oct. 23, 2017), https://blogs.fda.gov/fdavoice/index.php/2017/10/fda-taking-new-steps-to-better-inform-physicians-about-biosimilars-through-education-about-these-potentially-cost-saving-options/

but that "there is no anticipated 'automatic' market growth for biosimilars" because state substitution laws do not apply to them).

E. The biosimilars industry is at a critical juncture.

Although Congress passed the BPCIA in 2010, the biosimilars industry only started gaining momentum in 2015, when FDA published several important guidances implementing the statute and approved, in December of that year, the first biosimilar. Thus, the industry is still in its relative infancy. As of December 2017, FDA had approved nine biosimilars, including, in April 2016, Inflectra.[18] However, more biosimilar approvals are on the horizon. FDA has reported that as of April 2017, 66 biosimilars are in active development. Biosimilars Council at 2, n.vi (citing FDA sources). FDA has also received requests from potential biosimilar manufacturers for pre-development meetings involving 23 different RLDs. *Id.* at 2, n.vii (citing FDA sources).

Maintaining this momentum, however, depends on preserving fair, unfettered price competition in biologics markets. If brand name drug companies are able to prevent competition by unfairly blocking market access or discouraging insurers' and providers' use and reimbursement of approved biosimilars, biosimilar manufacturers will fail to capture the market share that befits FDA's finding of clinical similarity (or interchangeability). Failure to capture adequate market share will thus dramatically reduce biosimilar manufacturers' incentives to undertake the costly, time-consuming processes of biosimilar development and marketing. In short, if Congress's and the BPCIA's goals of savings to the healthcare system and increased

[18] FDA Biosimilar Product Information, *FDA-Approved Biosimilar Products*, https://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm580432.htm (last visited Jan. 26, 2018). Several of these approvals have been for biosimilar versions of the same RLD. In total, FDA has approved biosimilar versions of six branded biologic products. *Id.*

patient access to affordable medicines are to be met, it is critical at this early stage of the biosimilars industry that the incentives for biosimilar development and marketing be protected and reinforced, and that brand name drug companies be prevented from using exclusionary tactics that stifle fair price competition in the marketplace and, ultimately, harm patients and consumers nationally.

ARGUMENT

Defendants' exclusionary conduct threatens the long-term viability of the biosimilars industry.

The allegations in Pfizer's complaint – which must be taken to be true at the pleading stage – claim that Defendants have engaged in a broad-based scheme to block Inflectra from fairly competing in the marketplace with Remicade. *See generally* Compl. ¶¶ 55-79. Defendants have implemented this scheme, which J&J euphemistically titled its "Biosimilars Readiness Plan," through:

1. Exclusive dealing contracts with health insurers that either (1) require insurers to deny coverage for Inflectra altogether or (2) impose unreasonable preconditions (like a "fail first" requirement) governing coverage for Inflectra. *E.g.*, Pfizer Mem. Opp'n 6; Compl. ¶¶ 8, 58-64. J&J coerces insurers into these agreements by denying insurers rebates for Remicade unless they refuse to cover Inflectra. *E.g.*, Pfizer Mem. Opp'n 7; Compl. ¶¶ 9, 66.
2. Bundling arrangements through which J&J only provides rebates on *other products* if insurers agree not to cover Inflectra. *E.g.*, Pfizer Mem. Opp'n 8; Compl. ¶¶ 9, 67.

3. Exclusionary agreements and bundling arrangements with healthcare providers similar to those entered into with insurers. *E.g.*, Pfizer Mem. Opp'n 9; Compl. ¶¶ 11, 73.

J&J's "Biosimilars Readiness Plan," which Defendants do not deny conceiving or executing, would have profound implications for the future of biosimilars generally if left unchecked in this case. Indeed, Defendants' strategy could serve as a blueprint for *every* brand name biologic drug maker seeking to maintain monopoly power and profits indefinitely in the face of competition from a lower-priced biosimilar.

As Pfizer cogently explains in its opposition to the motion to dismiss, Defendants' exclusionary strategy rests on the fact that Remicade, like other brand name biologics threatened with current or imminent competition from biosimilars, has long enjoyed a monopoly in the relevant product market – in this case, the market for infusion-administered therapies for chronic conditions like Crohn's disease, ulcerative colitis, and rheumatoid arthritis. As a result of Remicade's longstanding monopoly, J&J has a stable base of patients who are unlikely ever to switch to a biosimilar. Pfizer Mem. Opp'n 7 (describing "installed base" of patients using Remicade). As alleged in the complaint, J&J leverages this "incontestable" patient base by denying rebates to insurance companies for *current*, incontestable patients using Remicade unless the insurers agree not to cover Inflectra for *new and future*, "contestable" patients – *i.e.*, the subset of patients who if given the opportunity might actually choose the lower-priced, highly similar Inflectra over Remicade.

A 2017 article published in the Journal of the American Medical Association and attached hereto as Exhibit 1 explains this "rebate trap." In short, in any case where the rebates offered by the brand company on the condition that insurers not cover the biosimilar are worth

more than the price savings offered by the biosimilar, insurers will have an economic incentive to accept the exclusionary agreements. *See* JAMA at 2163-64 and Table (demonstrating through a hypothetical example that insurers would be incentivized to accept exclusionary rebate deals even in the unlikely event that 50% of patients switched to the biosimilar). Because biosimilars often cannot capture sales to patients that are part of the branded product's "installed base," it is generally unlikely that the price savings from the biosimilar will exceed the value of the rebates. *See id.* at 2164 (noting that for many chronic diseases, the proportion of patients new to a given biologic therapy is less than 20% of the total patients taking that drug in a given year) (citation omitted). The "rebate trap," if not addressed in this case, could become a common feature of the biosimilar/RLD competitive landscape.

Similarly, J&J and other brand companies can leverage their patient bases for *other products* that enjoy strong brand loyalty by denying rebates to insurance companies for those products unless the insurers agree not to cover the relevant biosimilar. As Pfizer explains, RPS's' arrangements with insurers also have "spillover effect[s]" (Pfizer Mem. Opp'n at 8) on providers (such as hospitals) in cases of drugs that providers purchase and administer directly − a category that includes many other biologics in addition to Remicade. In those cases, providers that are unsure whether an insurance company will reimburse them for the drug will hesitate to stock (at their own cost) or prescribe that drug – even for patients who may be open to using the lower-priced biosimilar. The same principles apply to J&J's exclusionary agreements with providers themselves. These agreements use the threat of reduced rebates on Remicade (or other J&J products) to discourage providers from purchasing Inflectra for the subset of their patients (mostly new patients) who do not have the same brand loyalty to Remicade and might prefer the lower-priced Inflectra.

The net effect of these exclusionary practices, as Pfizer explains, is to deny consumers, insurers, and providers any real choice between Inflectra and Remicade − thereby undermining the public health goal of fair and robust price competition, and thus patient access, for biologic medicines that lies at the heart of the BPCIA. The irony is apparent: J&J's strategy to block competition from an approved biosimilar rests on and exploits the longstanding monopoly advantages that Congress sought to remedy through the BPCIA's expedited biosimilar approval pathway.

But the problem does not end with Remicade. Because many other high-priced biologics, like Remicade, have also enjoyed longstanding market exclusivity, during which they have developed entrenched customer bases that can be leveraged to coerce insurers and providers into limiting *new patients'* access to competing biosimilars, J&J's strategy for Remicade can easily be replicated for these other RLDs. As Pfizer's complaint notes (*e.g.*, ¶ 56), the J&J strategy has received significant attention in the biologics industry. Indeed, it is no exaggeration to say that this strategy, if permitted, will become the model for how high-priced branded biologics deal with the onset of biosimilar competition. Thus, the consequences of J&J's "Biosimilars Readiness Plan," if upheld by this Court, for the biosimilars industry *as a whole* would be dire.

Moreover, while J&J argues that the rebate arrangements it enters into with insurers and providers benefit consumers (even though Inflectra is priced lower than Remicade and, as alleged in Pfizer's complaint, Remicade's price has increased since Inflectra was introduced), this argument ignores the massive long-term harm to the BPCIA incentive structure caused by J&J's exclusionary strategy. This harm cannot be overstated. The BPCIA rests on the premise that an approved biosimilar can gain significant market share because of the price advantages

that result from expedited FDA review/approval, leading to massive savings for the U.S. healthcare system and increased patient access to life-saving medicines.

If, however, an approved biosimilar is prevented from competing on price terms because of the kinds of exclusionary arrangements at issue in this case, its market share will remain artificially small – as in the case of Inflectra, which has captured a mere 4% of the infliximab market. Compl. ¶ 102. Artificially low market share results, of course, in less-than-anticipated return on investment, which in turn diminishes the economic incentives needed to encourage drug companies to devote the considerable time and expense associated with developing and marketing biosimilars. Thus, J&J's tactics not only diminish competition in the specific market where those tactics are used; they also discourage future competition from biosimilars in any market where those tactics *could be* used in the future. The end result would be far fewer biosimilars, leading to far less competition from these expensive prescription drugs, and far less savings to the U.S. healthcare system, and, most tragically, continued limited access to life-saving medicines for patients who cannot afford expensive brand name biologics – all directly contrary to Congress's purpose in enacting the BPCIA.

The threat of diminished incentives for biosimilars comes at a time when there are few approved biosimilar products, but many biosimilars at various stages of development. *Supra* pp. 10-11. As noted above, the BPCIA provided RPS's with 12 years of statutory marketing exclusivity in exchange for agreement on an expedited biosimilar approval pathway. 42 U.S.C. § 262(k)(7)(A); *Amgen*, 137 S. Ct. at 1670. With time, more biologics that currently make outsized, blockbuster profits because they have the market all to themselves will fall outside this 12-year window, and FDA will be able to approve biosimilar versions of these products. *See* Biosimilars Council at 3-4 (citing Alavere Health study and noting that by 2025, seven

blockbuster branded biologics that taken together account for 30% of U.S. biologic sales will all be outside the 12-year exclusivity window). *See also* JAMA at 2163 (noting that biologics accounting for an estimated $100 billion worth of annual sales are set to lose patent exclusivity in the United States by 2020).

It is critical at this pivotal time for the fledgling biosimilars industry, and consistent with the overarching purposes of the BPCIA, that incentives to develop and market biosimilars remain strong to improve patient access to more affordable prescription drugs. Allowing J&J's "Biosimilars Readiness Plan" to continue, and to serve as a blueprint for stifling competition from affordable, safe, effective biosimilars, will have precisely the opposite effect: It would harm the public health by threatening patient access to more affordable, FDA-approved biologic medicines.

CONCLUSION

For the foregoing reasons, this Court should deny Defendants' motion to dismiss.

Dated: January 26, 2018

Respectfully submitted,

/s/ Steven N. Herman

Steven N. Herman (Bar No. 205832)
William B. Schultz
(*pro hac vice* motion to be submitted)
Carlos T. Angulo
(*pro hac vice* motion to be submitted)
ZUCKERMAN SPAEDER LLP
1800 M St, NW
Washington, DC 20036
Tel: 202-778-1800
Fax: 202-822-8136
sherman@zuckerman.com
wschultz@zuckerman.com
cangulo@zuckerman.com

Counsel for Proposed Amicus Curiae

CERTIFICATE OF SERVICE

I hereby certify that on this 26th day of January, 2018, I electronically filed the foregoing [PROPOSED] BRIEF OF THE BIOSIMILARS COUNCIL AS *AMICUS CURIAE* IN OPPOSITION TO DEFENDANTS' MOTION TO DISMISS by using the CM/ECF system. All parties to the case have been served through the CM/ECF system.

/s/ Steven N. Herman
Steven N. Herman

EXHIBIT 1

VIEWPOINT

Obstacles to the Adoption of Biosimilars for Chronic Diseases

Aaron Hakim, MS
Yale University School of Medicine, New Haven, Connecticut.

Joseph S. Ross, MD, MHS
Section of General Internal Medicine and Robert Wood Johnson Foundation Clinical Scholars Program, Yale University School of Medicine, New Haven, Connecticut; and Center for Outcomes Research and Evaluation, Yale-New Haven Hospital, New Haven, Connecticut.

Corresponding Author: Joseph S. Ross, MD, MHS, Section of General Internal Medicine, Yale University School of Medicine, PO Box 208093, New Haven, CT 06520-8093 (joseph.ross@yale.edu).

Biologic agents have an increasingly important role in clinical care, accounting for 22% of new US Food and Drug Administration (FDA) drug approvals from 2010-2015 and comprising 28% of overall prescription drug revenue in 2015.[1] Biologics are generally made from living organisms and are larger, more complex molecules than conventional small-molecule drugs. Commonly used biologics include adalimumab (Humira), etanercept (Enbrel), and infliximab (Remicade), protein-based drugs used to treat rheumatologic diseases. With the goal of facilitating competition and generating cost savings for consumers, the Biologics Price Competition and Innovation Act, part of the Affordable Care Act, authorized an approval pathway for "biosimilars." These are therapies with an active ingredient considered by the FDA to be highly similar to a reference biologic, such that there are no clinically meaningful differences in terms of safety, purity, and potency. Biosimilars can only be marketed after the reference biologic loses patent exclusivity.

In 2015, the FDA approved the first biosimilar, a version of the leukocyte growth factor filgrastim (Neupogen). Three more unique biosimilars—infliximab-dyyb, adalimumab-atto, and etanercept-szzs—frequently used for the treatment of multiple inflammatory conditions, including rheumatoid arthritis, inflammatory bowel disease, and psoriasis, were approved in 2016. Collectively, these 4 biosimilars have been approved to treat 23 different clinical indications, and in aggregate the branded biologic drugs accounted for $18.8 billion in US sales in 2015.[2] Biologics accounting for an estimated $100 billion worth of annual sales are set to lose patent exclusivity in the United States by 2020.[1]

There is optimism that biosimilars will offer lower-cost therapeutic alternatives to branded biologic drugs, in the same manner as generic drugs have done for small-molecule drugs. On average, the cost of a small-molecule drug declines by 70% in the 24 months following initial generic approval.[3] Furthermore, generic drugs currently account for 88% of all US prescriptions, yielding 10-year cost savings in excess of $1.5 trillion.[1] This Viewpoint explores why biosimilars for chronic diseases, the largest category of biological therapies, are unlikely to yield widely expected cost savings.

First, when a physician writes a prescription for a small-molecule drug, all states now have laws that either allow or require pharmacists to automatically substitute approved generic equivalent drugs, unless the physician has explicitly prohibited substitution. As a consequence, even without sales and marketing support, lower-priced generics typically gain substantial market share through automatic substitution. However, these state laws do not currently apply to biosimilars. Even though biosimilars are considered highly similar to reference biologics, they may have minor variations in well-characterized, clinically inactive components. Thus, there is no anticipated "automatic" market growth for biosimilars. Patients will require new prescriptions to be switched from branded biologics to biosimilars.

Second, when small-molecule generic drugs are first approved, payers often exclude the more expensive brand-name medication from payer formularies, or at least impose substantial cost-sharing requirements. However, this is unlikely to occur for branded biologics, in part because there is strong patient and physician aversion to requiring patients stabilized with branded biologics to switch to biosimilars for cost-saving purposes.[4] Although there is no clinical or physicochemical evidence for switch-related immunogenicity for any of the 4 FDA-approved biosimilars, any such effect would place patients at risk for worsened disease control.[5,6] Thus far, payers appear reluctant to use formulary utilization management strategies to promote the use of biosimilars for chronic disease treatment. For instance, infliximab (Remicade), a branded biologic used for the treatment of inflammatory conditions, has not been excluded from any large 2017 formularies despite the FDA approval of a biosimilar at a 15% discount to the wholesale acquisition cost of the brand.

Third, and most important, rebate agreements between pharmaceutical companies, pharmacy benefit managers, and other payers create an incentive for payers to prefer more expensive branded biologics over biosimilars. Most pharmaceutical companies currently provide rebates to pharmacy benefit managers to support preferred position of their branded biologic drugs on payer formularies.[7] In many biologic drug categories, such as the branded anti–tumor necrosis factor antibodies, rebates can reach up to 50% of the drug's list price. If a biosimilar manufacturer intends to upend the preferred position of the brand by offering a substantial price discount to the payer, the branded manufacturer can respond by withdrawing the rebate on the reference biologic, creating a "rebate trap." For any patient continuing the reference biologic, a payer's costs for that patient will double once the rebate is withdrawn, as illustrated by the example (**Table**). Even in this optimistic scenario, in which the price of the biosimilar is 60% less than the price of the brand after rebates and discounts, if the payer is only able to convert 50% of its patient users to the biosimilar, the rebate trap ensures that payer total costs actually increase relative to costs prior to biosimilar availability.

To avoid the rebate trap, any strategy to reduce spending on biologics through adoption of biosimilars requires a near-complete switch of patient users from

Table. Example of the "Rebate Trap"[a]

	Pre-Biosimilar	Post-Biosimilar	
		50% of Patients Switch	100% of Patients Switch
Reference biologic list price, US $	50 000	50 000	50 000
Reference biologic postrebate price, US $	25 000	NA (no longer offering rebate)	NA (no longer offering rebate)
Biosimilar price, US $	NA	10 000	10 000
Patients taking branded biologic, No.	1000	500	0
Patients taking biosimilar, No.	NA	500	1000
Payer cost, US $	25 000 000	30 000 000	10 000 000

Abbreviation: NA indicates not applicable.

[a] A payer with 1000 patients taking a branded biologic therapy that costs $50 000 for chronic disease treatment, $25 000 after rebates, considers formulary coverage of a biosimilar. Even with a substantially less-expensive biosimilar priced at $10 000, if only 50% of patients switch to the biosimilar, total costs for the payer increase by $5 million after the manufacturer revokes the 50% rebate on the brand biologic.

the branded biologic to the biosimilar. However, for many chronic diseases, the proportion of patients new to a given biological therapy is less than 20% of the total patients taking that drug in a given year.[7] The remainder represents a stable base of patients whose disease is well-maintained while they are using current therapy and thus are unlikely to switch.

Several policy solutions may help ensure that savings from biosimilars can be realized, assuming that biosimilars are less expensive and are priced lower than branded biologics. The US biosimilars pathway allows the FDA to designate biosimilar products as "interchangeable," a higher standard than "biosimilarity." However, since 2013, only 21 states have passed laws allowing substitution by a pharmacist based on interchangeability. Moreover, the FDA released draft regulatory guidance in January 2017 outlining a case-by-case approach for determining whether a biosimilar could be designated as interchangeable, considering biocharacterization, analytical similarity, switching studies, and postmarketing data. With this guidance in place, automatic substitution laws in all states based on interchangeability could bolster competition, lower prices, and increase biosimilar availability for patients.

Second, to facilitate the uptake of noninterchangeable US biosimilars, treatment guidelines from physician organizations could recommend biosimilars as first-line agents and follow Europe's successful history of biosimilar adoption. The European Medicines Agency does not have a formal interchangeable designation for biosimilars; the decision for automatic substitution is left to individual member countries. Europe's decade-long experience with biosimilars, including more than 400 million patient-days of clinical experience,[5,6] suggests that substituting biosimilars for reference products will not adversely affect safety, immunogenicity or efficacy. A total of 22 unique biosimilars have been approved in Europe since 2006, and automatic switching has been implemented in multiple countries, including through government-run, "winner-take-all" competitive bidding processes that have yielded 66% reductions in price.[8]

Third, legislators could demand greater transparency on how rebates influence therapeutic choice for patients. Drug price transparency and accountability laws have recently been proposed in several states, including one enacted in Vermont in 2016. In addition to requiring manufacturers to provide information on drug price increases, these laws can improve understanding of rebate use, amounts, and how rebate dynamics can promote use of branded products and discourage biosimilars.

Many of the challenges currently being raised against biosimilar substitution are similar to arguments used against traditional generic drug substitution following the passage of the Hatch-Waxman Act in 1984. Small-molecule generic drugs are now broadly viewed as an appropriate substitution for brand-name pharmaceuticals. Once the same is true for biosimilars, the health care system will likely realize substantial savings.

ARTICLE INFORMATION

Published Online: May 1, 2017. doi:10.1001/jama.2017.5202

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Mr Hakim reports being previously employed by Great Point Partners, a health care investment company. Dr Ross reports receiving research support through Yale University from Medtronic and the FDA to study issues in postmarket medical device surveillance, from the FDA to establish the Yale-Mayo Clinic Center for Excellence in Regulatory Science and Innovation (CERSI), from Johnson & Johnson to develop methods for clinical trial data sharing, from the Centers for Medicare & Medicaid Services to develop measures for public reporting of hospital and physician quality, from the Blue Cross-Blue Shield Association to advance premarket evidence generation for medical products, and from the Laura and John Arnold Foundation to support the Collaboration on Research Integrity and Transparency at Yale.

Additional Contributions: We thank Sanket S. Dhruva, MD, Yale University, and Michael Solotke, BS, Yale University, for critical review of an earlier version of the manuscript. Neither was compensated for their efforts nor have any conflicts of interest to disclose.

REFERENCES

1. Sarpatwari A, Avorn J, Kesselheim AS. Progress and hurdles for follow-on biologics. *N Engl J Med*. 2015;372(25):2380-2382.

2. Company 2015 Annual Financial Reports (10-K). US Securities and Exchange Commission EDGAR website. https://www.sec.gov/edgar/searchedgar/companysearch.html. Accessed December 23, 2016.

3. Berndt ER, Aitken ML. Brand loyalty, generic entry and price competition in pharmaceuticals in the quarter century after the 1984 Waxman-Hatch legislation. *Int J Econ Bus*. 2011;18(2):177-201.

4. The Alliance for Safe Biologic Medicines. Position statement 2015. https://safebiologics.org/2015/09/asbm-statement-on-fda-draft-guidance-nonproprietary-naming-of-biological-products/. Accessed April 25, 2017.

5. Zineh I, Christl LA. The biosimilarity concept: toward an integrated framework for evidence assessment. *Ann Intern Med*. 2016;165(8):595-596.

6. Braun J, Kudrin A. Switching to biosimilar infliximab (CT-P13): evidence of clinical safety, effectiveness and impact on public health. *Biologicals*. 2016;44(4):257-266.

7. Federal Trade Commission Follow-on Biologics Workshop, February 4, 2014. https://www.ftc.gov/news-events/events-calendar/2014/02/follow-biologics-workshop-impact-recent-legislative-regulatory. Accessed April 25, 2017.

8. Meek T. Nordic countries near complete switch to biosimilar Remicade. APM Health Europe. May 2, 2016. http://www.apmhealtheurope.com/Nordic-countries-near-complete-switch-to-biosimilar-Remicade-FS_47642.html. Accessed April 26, 2017.