IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civil Action No. 23-931-CFC

OPENING BRIEF IN SUPPORT OF PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

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Dated: September 26, 2023

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INTRODUCTION

It is an enduring principle of law that an agency tasked with implementing a regulatory program must adhere to the text of the statute. So too must Congress legislate within the bounds of the Constitution. This case involves distinct violations of both of these maxims.

This lawsuit involves the Medicare Drug Price Negotiation Program created by the Inflation Reduction Act of 2022 (IRA). The IRA enacted sweeping changes to drug pricing under Medicare, jettisoning a market-based approach in favor of a new scheme of federal price controls. Specifically, Congress created a drug price negotiation scheme that delegates to the Centers for Medicare & Medicaid Services (CMS) the authority to select drugs and biologics for purported "negotiation," and then to dictate a "Maximum Fair Price" (sometimes referred to as "MFP") that must fall under a statutory ceiling.

To be clear, there is no actual negotiation involved: A manufacturer may either consent to the agency's dictated price or face an extreme tax penalty of up to 95% of the drug's gross U.S. revenues on the drug – including non-Medicare sales. *Id.* § 1320f-5(a)(6); 26 U.S.C. § 5000D. Manufacturers thus have no real choice but to accede to the agency's unilaterally dictated price or terminate its Medicare Part D agreements and Medicaid rebate agreement, and not just for the drug in question, but for *all* of the manufacturer's drugs. To make matters worse, the IRA also purports

to preclude affected manufacturers even from seeking judicial review of key aspects of the program, such as the "selection of drugs" and the "determination of a maximum fair price." 42 U.S.C. § 1320f-7. Collectively, these provisions violate the procedural due process guarantees of the Fifth Amendment.

Further aggravating the issue, CMS imposed new policies through two guidance documents (the Guidance Documents) that far exceed the confines of the governing statute. The Guidance Documents violate the Administrative Procedure Act (APA) for at least two reasons: First, they override the statutory definition of "Qualifying Single Source Drug," such that the term impermissibly includes two different drugs approved at different times. Second, they add a new "bona fide marketing" requirement that sweeps drugs into the selection process and keeps the price controls in place even when they have generic competition. The agency's positions on these issues flout the IRA's text and violate basic APA principles.

The pharmaceutical industry expends vast amounts of time and the support of significant monetary investment to identify, test, and develop any new drug candidate. At the end of that process, very few early drug candidates are ever approved and commercialized. The most important constituents depending on the high-risk, low-probability drug development marathon are patients. Nowhere is this more apparent than in the context of drugs that treat orphan conditions, defined as those impacting fewer than 200,000 Americans or rare conditions. Because the

patient populations for these diseases are so small, innovator pharmaceutical companies take on enormous risks in developing new drug products and new indications for existing products.

The Medicare Drug Price Negotiation Program and its implementing regulations undermine the incentives for manufacturers to take on that risk. If a drug defies the odds and is approved, manufacturers may be forced to enter into a "negotiation" in which they have no leverage and no meaningful ability to challenge the resulting Maximum Fair Price. The agency's positions in the Guidance Documents introduce even further risks for manufacturers not even grounded in the statute itself: Their separate drug products may be consolidated and treated as one, and generic competition for their products may be ignored by CMS in implementing the statute. All of this undermines innovation and the discourages the development of new treatment options, in turn threatening patients' access to new therapies.

AstraZeneca brought this case to rectify those legal wrongs. AstraZeneca must enter into an agreement to "negotiate" by October 1, 2023. It then must respond to an initial offer from CMS by March 2, 2024. AstraZeneca therefore sought – and the Court agreed to – expedited briefing in this administrative record-based case to allow for a final decision on or before **March 1, 2024**.

STATEMENT OF UNDISPUTED FACTS

The Medicare program, enacted in 1965, provides health insurance for individuals 65 years of age and older, some individuals with disabilities, and individuals with certain conditions such as end-stage renal disease. Medicare Part B covers enrolled beneficiaries for, in relevant part, drugs and biological products administered by physicians and other health care providers.[1] Medicare Part D, which is optional, helps cover enrolled beneficiaries for the cost of self-administered drugs. Approximately 20 percent of all Americans are covered by Medicare, and Medicare pays for approximately 40 percent of all prescription drug sales.

All "new drugs" must be approved by FDA before being introduced into interstate commerce. 21 U.S.C. §§ 355(a), 331(d). A "new drug" may be a drug product that has never been approved, or it may be an approved drug product with a change, such as a new intended use or indication, or a different strength or dosage form. 21 U.S.C. § 321(p). Innovator drugs are typically approved under a New Drug Application (NDA) or a Biologics License Application (BLA).

Innovator drug manufacturers invest tremendous resources pursuing new drug candidates in the hopes that they might provide new therapeutic options for patients

[1] In FDA parlance, a "biological product" includes drug products that are made from a virus, therapeutic serum, toxin, vaccine, blood, protein, or certain other similar products. 42 U.S.C. § 262(i).

that can save their lives, or at least make them better. The process is arduous, however, and only a scant few early drug candidates are ever approved and commercialized. Studies estimate that only one out of every 5,000 compounds that enters preclinical testing will achieve FDA approval – a failure rate of 99.98%. For that reason, innovator drugs are often rewarded with periods of marketing exclusivity and patent rights, including a seven-year period of market exclusivity for orphan drugs. 21 U.S.C. § 360aa *et seq*. Historically, these manufacturers have been able to sell their products both commercially and under Medicare at prices dictated by market dynamics. That market-driven dynamic has now come to a crashing halt with the passage of the IRA.

The IRA

In August 2022, President Biden signed the IRA, which made sweeping changes to health care, tax, and climate laws. Relevant here, the IRA provides for a "Drug Price Negotiation Program" that lowers the Medicare Parts B and D prices of certain drugs and biologics lacking generic or biosimilar competition.[2]

[2] Just as a generic drug enters the market by piggybacking on an innovator drug's FDA approval status, a "biosimilar" "is a biologic product that is highly similar to a biologic product that has already been approved by" FDA and thus references the already-approved biological product to gain FDA approval. *Sandoz Inc. v. Amgen Inc.*, 582 U.S. 1, 5 (2017).

Each year, HHS must select a specified number of "negotiation-eligible" drugs with the highest total Medicare Part B or D expenditures over a specified preceding 12-month period. 42 U.S.C. § 1320f-1(b)(1)(A). CMS must rank these "negotiation-eligible" drugs in order of the highest total Medicare expenditures during that period and must select an increasing number of the highest ranked drugs for the Program each year. *Id.* § 1320f-1(a)-(b). The number of drugs selected for price-setting is cumulative.

CMS has selected ten Part D drugs for 2026, the first price applicability year. AstraZeneca's drug product FARXIGA® (dapagliflozin) – a highly effective treatment for diabetes, heart disease, and chronic kidney disease – was on that list. Ex. 3, *HHS Selects the First Drugs for Medicare Drug Price Negotiation* (Aug. 29, 2023), *available at* https://www.hhs.gov/about/news/2023/08/29/hhs-selects-the-first-drugs-for-medicare-drug-price-negotiation.html. CMS will select up to 50 additional drugs over the next three years. That selection gauntlet is all but certain to sweep up more AstraZeneca products that patients with life-threatening or life-altering illnesses depend upon.

To be eligible for selection and negotiation, a drug must be a "Qualifying Single Source Drug." 42 U.S.C. § 1320f-1(d)(1). That term is expressly defined in the statute, and the definition has several parts. First, for the first year (IPAY, in IRA parlance), the drug must be "a covered part D drug (as defined in section

1395w-102(e) of this title [the Medicare statute])." 42 U.S.C. § 1320f-1(e)(1). Second, the drug must be FDA-approved, and at least 7 years must have elapsed "since the date of such approval." *Id.* § 1320f-1(e)(1)(A). And third, the drug must not be the reference listed drug for a generic drug that has been "approved and marketed." *Id.*

Once a manufacturer's drug is selected for negotiation, the manufacturer must enter into an agreement to negotiate the price of the drug. 42 U.S.C. § 1320f-3(a). The agency then purportedly "negotiate[s]" with the manufacturer over a "maximum fair price" for the selected drug, with the agency ultimately having the final say with a take-it-or-leave-it offer. *Id*. The IRA directs CMS to "develop and use a consistent methodology and process . . . for negotiations . . . that aims to achieve the lowest maximum fair price for each selected drug." *Id.* § 1320f–3(b)(1).

The statute freezes the "maximum fair price" in place: Once a product is selected and CMS assigns it an MFP, the manufacturer cannot sell its product above the ceiling price unless and until a generic drug or biosimilar is "approved and marketed." 42 U.S.C. §§ 1320f–1(e)(1)(A)(iii), (B)(iii).

This is a negotiation in name only, however, and the "maximum fair price" contemplated by the IRA is neither maximum nor fair. The price is capped at a fraction of reference prices specified by statute and defined by the Guidance to be as low as possible, and the agency can insist that the "maximum fair price" be set

lower than the cap. 42 U.S.C. § 1320f-3(c). The "maximum fair price" will be adjusted each subsequent year by an inflation factor for a specified preceding 12-month period. Ex. 2, CMS, *Medicare Drug Price Negotiation Program: Revised Guidance, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026*, at 162 (June 30, 2023) (Final Guidance).

Once CMS has imposed a maximum fair price for a selected drug, the manufacturer must provide "access to such price" to a variety of Medicare-eligible individuals and entities. 42 U.S.C. § 1320f–2(a)(1). These participants include all eligible Medicare beneficiaries who are dispensed drugs under Medicare Parts B and D; all "pharmacies, mail order services, and other dispensers" that dispense drugs to Medicare beneficiaries; and all "hospitals, physicians, and other providers of services and suppliers" that furnish or administer drugs to Medicare beneficiaries. *Id.* §§ 1320f–2(a)(1)(A)-(B); *see id.* § 1320f(c)(2). Manufacturers that fail to provide the required access to the maximum fair price are subject to a civil monetary penalty of ten times the difference between the price the manufacturer actually charges and the maximum fair price, multiplied by the total number of units sold. *Id.* § 1320f–6(a).

None of this process occurs at arm's length. Any manufacturer that declines to enter into negotiations, or declines to agree with CMS on a "maximum fair price," is subject to penalty in the form of an escalating excise "tax." 26 U.S.C. § 5000D(b).

This tax can be as high as 95% of the *total* U.S. revenues for the drug. *Id.* § 5000D(a). The penalty also accrues daily until the manufacturer accedes to the agency's "maximum fair price" (or until the drug in question ceases to be a selected drug). *Id.*

The penalty is calculated based on an "applicable percentage," which starts at 65% and increases by 10% for each successive quarter that the manufacturer is out of compliance, to a maximum of 95%. *Id.* § 5000D(d). The statute provides that the penalty is "in an amount such that the applicable percentage is equal to the ratio of . . . (1) such tax, divided by (2) the sum of such tax and the price for which so sold [sic]." *Id.* § 5000D(a). The excise-tax penalty thus represents a multiple of the manufacturer's total revenues from the drug in question, not merely its profits.

The IRA provides for the "[s]uspension" of the excise-tax penalty, but only if the manufacturer terminates its Medicare Part D agreement and Medicaid rebate agreement – not just for the drug in question, but for all of the manufacturer's drugs. 26 U.S.C. § 5000D(c); *see id.* § 5000D(c)(1). Thus, to suspend application of the tax penalty, a pharmaceutical manufacturer must entirely cease participation in both Medicare and Medicaid. This is not a viable option for any manufacturer, given that these programs collectively cover more than a third of the U.S. population. *See Sanofi Aventis U.S. LLC v. HHS*, 58 F.4th 696, 699 (3d Cir. 2023) (noting that these programs represent approximately half of all pharmaceutical sales).

Manufacturers that disagree with the selection of their drug or with the price dictated by CMS are nominally out of luck. Congress included in the statute a provision purporting to preclude judicial review for certain key aspects of the Drug Price Negotiation Program, including the "selection of drugs," the "determination of qualifying single source drugs," and the "determination of a maximum fair price." 42 U.S.C. § 1320f-7.

CMS Guidance

On March 15, 2023, CMS issued an initial guidance document detailing how the agency planned to execute these changes for the first year of the program. Ex. 1, CMS, *Medicare Drug Price Negotiation Program: Initial Memorandum, Implementation of Sections 1191-1198 of the Social Security Act for Initial Price Applicability Year 2026* (Mar. 15, 2023) (Initial Guidance). Portions of the Initial Guidance covering the first year of the Program became final immediately, without a comment period.

On June 30, 2023, CMS released another guidance document representing the agency's final word on implementation of the Drug Price Negotiation Program's first year. Ex. 2.

The Guidance Documents violate the agency's statutory mandate under the IRA in at least two ways.

First, CMS altered the requirements that must be met before a drug is deemed to have generic competition. The IRA sets up two alternative pathways for moderating drug prices: market-based competition in the form of a generic or biosimilar competitor, or failing that, price controls. The IRA specifies two objective criteria for a generic drug or biosimilar to render a brand name drug ineligible for selection and negotiation: the generic drug must be "approved" (or, in the case of a biologic, "licensed") and it must be "marketed." 42 U.S.C. §§ 1320f-1(e)(1)(A)(iii), (B)(iii). In its Guidance Documents, however, CMS created a new and fundamentally different test: CMS will subjectively assess the generic or biosimilar biological product in order to determine whether it has been the subject of "*bona fide* marketing." Not only will CMS apply that subjective test in making an initial determination of generic marketing, but the agency will continue to monitor the generic's status over time, post-entry, to ensure that it is consistently satisfying the "*bona fide* marketing" test. Ex. 1 at 62, 67; Ex. 2 at 101–102 (emphasis added).

Second, CMS redefined the term "Qualifying Single Source Drug." Under the statute, whether a drug constitutes its own Qualifying Single Source Drug depends on whether it has been approved under a separate NDA or BLA. 42 U.S.C. § 1320f-1(e). In its Guidance Documents, however, CMS defined a Qualifying Single Source Drug to embrace *all* dosage forms and strengths of *any* drug marketed

by the manufacturer with the same active moiety or ingredient – expanding the universe of products that are treated as a single "drug." Ex. 1 at 8 (defining a Qualifying Single Source Drug as "all dosage forms and strengths of the drug with the same active moiety and the same holder of an [NDA], *inclusive of products that are marketed pursuant to different NDAs*") (emphasis added); *see also* Ex. 2 at 99.

The agency's recasting of the term has material consequences for manufacturers: Two products approved under different NDAs with the same active moiety – including one approved years after the first, after extensive research and financial investment – will now run on the same selection clock, based on the approval or licensure date of the earlier approved product. Medicare expenditures on both products will be aggregated for purposes of ranking the qualifying single source drug for selection for negotiation. In addition, the negotiated maximum fair price will apply across both products – including to the new product as soon as it is approved. Ex. 1 at 59. This unsupported and overly expansive reading of the IRA harms drug manufacturers – and more important, it harms patients by disincentivizing future investment in new therapies.

AstraZeneca filed this lawsuit in August 2023. The following week, HHS announced the first ten drugs the agency had selected for negotiation. AstraZeneca's drug FARXIGA was on the list.

STANDARD OF REVIEW

"[W]hen a party seeks review of agency action under the APA, the district judge sits as an appellate tribunal." *American Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1083 (D.C. Cir. 2001). Because "the entire case on review is a question of law," *Marshall Cnty. Health Care Auth. v. Shalala*, 988 F.2d 1221, 1226 (D.C. Cir. 1993), "[t]he customary summary judgment standard does not apply," *Bintz v. Federal Emergency Mgmt. Agency*, 413 F. Supp. 3d 349, 360 (D. Del. 2019).

Instead, the APA supplies the applicable standard: courts "shall 'hold unlawful and set aside agency action' that is 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law' . . . or 'without observance of procedure required by law.' " *AstraZeneca Pharms. LP v. Becerra*, 543 F. Supp. 3d 47, 54 (D. Del. 2021) (quoting 5 U.S.C. §§ 706(2)(A), (C) & (D)).

Agency action violates the APA when it contravenes the text of an agency's governing statute. *See Natural Res. Def. Council v. EPA*, 643 F.3d 311, 323 (D.C. Cir. 2011); *Orion Rsrvs. Ltd. P'ship v. Salazar*, 553 F.3d 697, 703 (D.C. Cir. 2009); *Delaware Div. of Health & Soc. Servs. v. HHS*, 665 F. Supp. 1104, 1128 (D. Del. 1987).

In addition, agency action is unlawful under the APA when it is arbitrary and capricious. That happens when the agency fails to adequately explain a deviation from prior policy, *Steenholdt v. FAA*, 314 F.3d 633, 639 (D.C. Cir. 2003), or ignores

evidence bearing on the issue, *Butte Cnty. v. Hogen*, 613 F.3d 190 (D.C. Cir. 2010). Agency action also is arbitrary and capricious when the agency entirely "fail[s] to consider an important aspect of the problem, offer[s] an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co*., 463 U.S. 29, 43 (1983).

CMS has violated all of these requirements here.

ARGUMENT

I. CMS' QUALIFYING SINGLE SOURCE DRUG DEFINITION IS UNLAWFUL.

Under the IRA, two drug products are the same Qualifying Single Source Drug *only* where the two products were approved by FDA under the same NDA or BLA. The agency's Guidance Documents, however, take the position that two separate drug products with the same active moiety or active ingredient are treated as the same Qualifying Single Source Drug, even if they were approved under distinct NDAs or BLAs. Ex. 1 at 8; Ex. 2 § 30.1 at 99 (extending term to "all dosage forms and strengths of the drug with the same active moiety and the same holder of [an NDA], *inclusive of products that are marketed pursuant to different NDAs*") (emphasis added). The agency lacks the statutory authority to aggregate different drug products approved under different NDAs or BLAs into the same Qualifying Single Source Drug. Its rogue definition is also arbitrary and capricious.

A. Statutory Violation

The IRA provides its own definition of Qualifying Single Source Drug, and it controls here. The IRA's definition of that term cross-references the definition for a "covered part D drug" in the Medicare statute. 42 U.S.C. § 1320f-1(e)(1). That definition, in turn, cross-references the definition for a "covered outpatient drug" in the Medicaid Drug Rebate Program statute. *Id.* § 1395w-102(e)(1). Under *that* definition, whether a single source drug is a distinct "covered outpatient drug" is based on whether the product is approved pursuant to a distinct NDA or BLA. *Id.* §§ 1396r–8(k)(2), (k)(7)(A)(iv); *see also* 42 C.F.R. § 447.50.

The *only* exception to the MDRP's stance that a drug is defined by its NDA or BLA comes in the context of line extensions, which involve new formulations of a drug typically approved under a distinct NDA or BLA. Congress specifically amended the MDRP statute to treat line extensions as the same "covered outpatient drug" even if they were approved under different NDAs or BLAs. Patient Protection and Affordable Care Act of 2010, § 2503, Pub. L. No. 111-148, 124 Stat. 119 (codified at 42 U.S.C. § 1396r–8(c)(2)(C)). Tellingly, Congress chose *not* to include this exception in the IRA's drug pricing negotiation program, but *did* expressly do so in the IRA's Part D inflation rebate provision. 42 U.S.C. § 1395w–114a(g)(1)(B). Congress must be presumed to have acted deliberately in doing so. *Sosa v. Alvarez-Machain*, 542 U.S. 692, 711 n.9 (2004) ("[W]hen the legislature uses certain

language in one part of the statute and different language in another, the court assumes different meanings were intended.").

That is not the only textual clue that a Qualifying Single Source Drug must be defined by its NDA or BLA number. The IRA further defines a Qualifying Single Source Drug as a drug approved by FDA and for which "at least 7 years will have elapsed since the date of *such approval*." 42 U.S.C. § 1320f-1(e)(1)(A) (emphasis added). The definition is the same for a biological product, except the applicable time period requires that "at least 11 years will have elapsed since the date of *such licensure*." 42 U.S.C. § 1320f-1(e)(1)(B) (emphasis added). This language directs that each Qualifying Single Source Drug must be identified by reference to its *individual* approval or licensure, i.e., its distinct NDA or BLA. Any other reading – including the one based on common active moiety or common active ingredient espoused by CMS – contradicts the plain text of the statute and therefore must be set aside. *See Natural Res. Def. Council*, 643 F.3d at 323; *see also Lone Mountain Processing, Inc. v. Secretary of Labor*, 709 F.3d 1161, 1164 (D.C. Cir. 2013).

The effects will be felt across AstraZeneca's product portfolio. AstraZeneca markets the cancer medication LYNPARZA® (olaparib), a small-molecule cancer medicine first approved in capsule form in 2014. Over time, AstraZeneca continued to invest in the drug, developing a formulation that was better tolerated by patients, resulting in FDA approval for a tablet form under a different NDA in 2017. The

tablet form expanded the patient population able to benefit from the active ingredient, because it could be taken with certain other medicines. Although the IRA itself demands that these products be viewed as different Qualifying Single Source Drugs, CMS's approach would commingle all separate drug products sharing the same active ingredient, even if they were approved under different NDAs. The same will be true of future single active ingredient drug products sharing the same active ingredient as FARXIGA: The later-approved drug products will become eligible for the MFP price cap as soon as they are approved – in violation of the plain language of the IRA. This not only undermines the statutory scheme, but it also disincentivizes manufacturers like AstraZeneca from pursuing new uses for existing active ingredients.

B. Arbitrary and Capricious.

CMS's position also is arbitrary and capricious. Under the agency's new policy, CMS will consolidate all of a manufacturer's drug products containing the same active ingredient or active moiety, even those later approved under a distinct application or licensure. It makes little to no sense for CMS to pull drugs into the queue for negotiation based on the approval date of another distinct drug product – let alone to apply the MFP to drug products approved by FDA under separate NDAs.

Among other things, the new product could be deemed eligible for selection *immediately* upon approval, if it comes more than 7 years after approval of the initial

product (11 years for a biological product). Under the agency's approach, the clock will begin to run from when FDA approved the *first* product with the same active moiety, rather than from the date of approval of the newer product, as Congress required. 42 U.S.C. § 1320f-1(e)(1)(A)(i)-(ii).

Once a drug is selected for negotiation, any new drug product containing the same active moiety will instantaneously be subject to the MFP the agency sets for the selected drug. The agency's approach thus incentivizes manufacturers not to innovate. That, too, is arbitrary and capricious. *Cf. Michigan v. EPA*, 576 U.S. 743, 753 (2015) ("reasonable regulation ordinarily requires paying attention to the advantages and the disadvantages of agency decisions"); *Verizon Commc'ns, Inc. v. FCC*, 535 U.S. 467, 551-554 (2002) (Breyer, J., concurring in part and dissenting in part) (agency action providing no "incentive" for "incumbents either to innovate or to invest," thus causing "investment [to] stagnate," was a problem "potentially severing any rational relation between the Commission's regulations and the statutory provision's basic purposes").

II. CMS'S "BONA FIDE MARKETING" STANDARD IS UNLAWFUL.

The agency also has overridden the statutory test for determining whether a generic drug disqualifies a reference drug from participation in the Drug Price Negotiation Program. Under the IRA, a drug is ineligible for selection if an FDA-approved generic drug is "approved and marketed" (or, in the case of a biologic,

"licensed and marketed"). 42 U.S.C. §§ 1320f-1(e)(1)(A)(iii)-(B)(iii). Nowhere in the law did Congress include qualifying language that might narrow or otherwise change the ordinary meaning of the word "marketed." *Id.*

CMS's Guidance, however, conflicts with the statutory text. The agency redefined the statutory term "marketed" to mean "bona fide market[ed]," creating a wholly new "totality of the circumstances" test that supplants the statute's objective inquiry. Ex. 1 at 10, 62; Ex. 2 at 72, 101–102. The agency's interpretation is unlawful, both because it violates the agency's statutory mandate and because it is arbitrary and capricious.

A. Statutory Violation.

The IRA demands that CMS ask and answer a categorical question: Is an approved generic drug or biosimilar "marketed"? If so, the reference listed drug (the innovator pharmaceutical product upon which generic competitors' FDA approvals are based) is ineligible for selection. 42 U.S.C. §§ 1320f-1(e)(1)(A)(iii)-(B)(iii). And if the generic or biosimilar launches after the reference drug has been selected for negotiation, the "marketed" determination either stops the negotiation process for the selected drug or cuts short the time period to which an MFP applies. 42 U.S.C. § 1320f-1(c)(1)(B).

The statute calls for an objective, check-the-box inquiry into whether a generic drug or biosimilar is "marketed," a statutory term with an accepted ordinary

meaning. "Marketed" means to "expose for sale in a market," Ex. 5 (Merriam-Webster Dictionary),[3] or "to bring or send to a market," Ex. 6 (Oxford English Dictionary).[4] The statute accordingly must be applied as written: If a generic or biosimilar is "marketed," the reference product cannot be conscripted into the IRA's Drug Price Negotiation Program or the application of any existing MFP must end. *See Prestol Espinal v. Attorney Gen. of U.S.*, 653 F.3d 213, 221 (3d Cir. 2011) (Courts " 'defer to an agency's efforts to fill statutory gaps, not to create them, and in this instance Congress left no gap to fill[.]' " (quoting *Pruidze v. Holder*, 632 F.3d 234, 240 (6th Cir. 2011))).

In its Guidance Documents, however, CMS attempted to override this statutory mandate. In the agency's view, a drug that faces generic competition in the market will still be treated as a Qualifying Single Source Drug and any applicable MFP will remain in place unless the marketing of the generic products rises to the level of "*bona fide* marketing," meaning that sellers must sell the product in a "robust and meaningful" manner. Ex. 1 at 67–68; Ex. 2 at 73. The "bona fide marketing" test is a subjective, multi-factor inquiry based on the "totality of the circumstances."

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[3] *Available at* https://www.merriam-webster.com/dictionary/marketed (last accessed Sept. 26, 2023).

[4] *Available at* https://www.oed.com/dictionary/market_v?tab=meaning_and_use&tl=true#38116584 (last accessed Sept. 26, 2023)

Ex. 1 at 62; Ex. 2 at 101–102. The agency plans to review data over a 12-month period and make a "holistic inquiry" based on the "totality of the circumstances" about "whether a generic drug or biosimilar is marketed on a bona fide basis." *Id.* The end result is that even a drug with generic competition on the market may be selected for negotiation and, if it is already subject to a Maximum Fair Price, remain subjected to that price, if CMS concludes that the drug's generic competition is not "bona fide" enough.

CMS also announced that even after it determines a generic drug is subject to bona fide marketing, it will monitor "whether meaningful competition *continues to exist* in the market by ongoing assessments of whether the manufacturer of the generic drug . . . is engaging in bona fide marketing." Ex. 2 § 90.4 at 170 (emphasis added). CMS intends to conduct such monitoring by reviewing a number of factors, including but not limited to "whether the generic drug or biosimilar biological product is regularly and consistently available for purchase through the pharmaceutical supply chain and whether any licenses or other agreements between a Primary Manufacturer and a generic drug or biosimilar manufacturer limit the availability or distribution of the selected drug." *Id.* CMS also intends to "analyze the share of generic drug or biosimilar biological product units identified in [Medicare claims] data as a percentage of total units of Part D expenditures, as well as whether manufacturers are reporting units of the selected drug as part of their

[Average Manufacturer Price (AMP)] reporting responsibilities under section 1927(b)(3)(A) of the Act, and the trend in reporting of such AMP units." *Id.* If CMS determines through monitoring that a generic drug manufacturer is not engaged in bona fide marketing after a previous determination that there was an approved and marketed generic, "the drug/biologic could be eligible for negotiation in a future price applicability year." *Id.* at 78.

The agency's subjective totality-of-the-circumstances standard is wholly divorced from the statutory text. "One can conceive of a statute in which Congress makes clear that the totality of the circumstances is always to be considered" – for example, in evaluating subjective concepts like whether a chapter 11 bankruptcy has been filed in "good faith," or whether there is "probable cause" for a search. Antonin Scalia, *The Rule of Law As A Law of Rules*, 56 U. Chi. L. Rev. 1175, 1183 (1989). But "unless such a statutory intent" to apply a totality-of-the-circumstances standard "is express or clearly implied, courts properly assume that 'categorical decisions may be appropriate and individual circumstances disregarded when a case fits into a genus in which the balance characteristically tips in one direction.' " *Id.* (quoting *Department of Just. v. Reporters Comm. For Freedom of Press*, 489 U.S. 749, 776 (1989)).

CMS is well aware of the plain and ordinary meaning of the statutory term "marketed." Indeed, another section of the *Initial* Guidance – the provision listing

the data that manufacturers must submit to CMS – defined "marketing" in accordance with that plain meaning: "[T]he introduction or delivery for introduction into interstate commerce of a drug product." Ex. 1 at 82. CMS deleted that definition in the *Final* Guidance without explanation, an implicit acknowledgement of the sharp contrast between the accepted, objective definition and CMS's new, entirely subjective "bona fide marketing" standard.

The agency also has interpreted the term "marketed" in other contexts as an objective, point-in-time inquiry. For example, for purposes of the IRA's Part D inflation rebates, CMS proposed to determine when a product is "marketed" by reference to its "market date" as reported under the Medicaid Drug Rebate Program (MDRP). Ex. 4 (CMS, Medicare Part D Drug Inflation Rebates Paid by Manufacturers: Initial Memorandum, at 18–19 (Feb. 9, 2023)). In turn, CMS's longstanding policy under the MDRP has been to define "marketed" by reference to the date on which a product "is available for sale." *Announcement of Medicaid Drug Rebate Program*, 83 Fed. Reg. 12,770, 12,784 (Mar. 23, 2018) (MDRP National Rebate Agreement); *see also* 42 C.F.R. § 447.502. That meaning is echoed in the agency's pending proposed MDRP rule, where CMS has proposed to define a drug's "market date" as the "date on which the . . . drug was first sold." *Updates Under the Medicaid Drug Rebate Program*, 88 Fed. Reg. 34,238, 34,292 (May 26, 2023).

Moving beyond CMS, this is legal ground that has previously been trod. The Supreme Court in *Asgrow Seed Co. v. Winterboer*, 513 U.S. 179 (1995), addressed whether an Iowa farming couple had planted and harvested seeds "as a step in marketing" under the Plant Variety Protection Act. *Id.* at 186. The Court noted that the word "marketing" refers to "the act of holding forth property for sale." *Id.* at 187 (citing dictionary definitions). In doing so, the Court rebuffed the Federal Circuit's attempt to read into the statute's use of "marketing" a requirement that the marketing be sufficiently robust or meaningful. *Id.* (noting that "the word [marketing] does not require that the promotional or merchandising activities connected with the selling be extensive"). By way of example, the Court explained that "[o]ne can market apples by simply displaying them on a cart with a price tag; or market a stock by simply listing it on a stock exchange; or market a house (we would normally say 'place it on the market') by simply setting a 'for sale' sign on the front lawn." *Id.* The term "marketed" is an objective standard, not a subjective one.

Nor can CMS find a foothold in statutory structure, as there is no contextual evidence that the enacting Congress could have intended this overlay. "Even if the word 'marketing' could, in one of its meanings, demand extensive promotion," there is "no reason why the law at issue here would intend that meaning." *Id.* CMS's

strained reading would also have "the effect of requiring courts to ponder the difficult question of how much promotion is necessary to constitute marketing." *Id.*

That sort of ponderous regime is especially unwarranted here, because Congress has shown it knows how to establish a subjective "bona fide" standard when it wishes to do so. *See* 42 U.S.C. § 1396r-8(k)(1)(B)(i)(II) (as amended by § 2503(a)(2), Pub. L. No. 111-148, 124 Stat. 119) (amending the Medicaid Drug Rebate Program statute to specify that only "bona fide" service fees are exempt from the calculation of average manufacturer price); § 1396r-8(e)(5) (as amended by § 2503(a)(1), Pub. L. No. 111-148, 124 Stat. 119) (amending the MDRP statute to direct the calculation of a drug's federal upper limit using "pharmaceutically and therapeutically equivalent multiple source drug products . . . available for purchase by retail community pharmacies on a nationwide basis"). Congress chose not to do that in the IRA, and that silence says something important: "Omitting a phrase from one statute that Congress has used in another statute with a similar purpose 'virtually commands the . . . inference' that the two have different meanings." *Prewett v. Weems*, 749 F.3d 454, 461 (6th Cir. 2014) (quoting *United States v. Ressam*, 553 U.S. 272, 276–277 (2008)). That is why when "Congress opts not to include a well known and frequently used approach in drafting a statute, the courts" – to say nothing of an agency – "should hesitate to pencil it back in under the guise of interpretation." *Id.*

Similarly, there is no statutory basis for CMS to conduct ongoing monitoring after a generic competitor is approved and marketed. Yet, the agency threatens to withdraw its prior determinations that a drug is disqualified from selection or price controls based on the agency's unilateral determination at some later time that there is insufficiently "meaningful" competition between the innovative and generic versions of a drug. Ex. 1 at 67–68; Ex. 2 at 74, 170. That, too, flatly violates the statute.

The agency's approach has real-world consequences for manufacturers like AstraZeneca. The statute mandates that generic competition will remove a drug from selection and exempt it from the Maximum Fair Price. Under the Guidance, however, CMS purports to hand itself discretion to refuse to recognize generic competition when it feels like it. That poses additional risk to manufacturers that is not permitted under the statute. The agency's "bona fide marketing" test constitutes agency overreach, and undermines the plain mandate from Congress.

B. Arbitrary and Capricious

The agency's "bona fide marketing" standard also is arbitrary and capricious. Agency action is arbitrary and capricious under the APA when the agency entirely "fail[s] to consider an important aspect of the problem, offer[s] an explanation for its decision that runs counter to the evidence before the agency, or is so implausible

that it could not be ascribed to a difference in view or the product of agency expertise." *State Farm*, 463 U.S. at 43.

The agency has signaled its intent to rely on Prescription Drug Event (PDE) data when making its "bona fide marketing" judgment calls. Ex. 1 at 10; Ex. 2 at 101–102. PDE data reporting, which contains exclusively Medicare Part D plans, moves at a glacial pace. One recent analysis found that Part D was "notably slower than commercial plans in coverage of first generics," so much so that in the 2021 Medicare Part D plan year, only 21% of first generics that launched in 2020 were covered by plan formularies. Worse still, "it takes nearly three years before first generics are covered on more than half of Medicare Part D formularies." Ex. 7 (Association for Accessible Medicines, *New Generics are Less Available in Medicare than Commercial Plans: New Evidence Shows Medicare Part D Plans Continue to Fail to Get New Generics to Seniors* (July 13, 2021)); *see also* Ex. 8 (Astellas Comment Letter (citing same)). That is why the agency allows Part D plans' Pharmacy and Therapeutics Committees a lengthy period to review new drugs before deciding whether to place them on formulary. *See* Ex. 9 (Medicare Prescription Drug Benefit Manual, ch. 6, § 30.1.5 (rev. Jan. 15, 2016)). As a result, the first six months of PDE data reported after a drug faces generic competition necessarily reflect very limited uptake.

That works a fundamental unfairness to regulated entities. As explained *infra*, the IRA is a heavy-handed statute that imposes a significant burden on manufacturers. The one critical concession the statute gives to manufacturers – and it does so unambiguously – is that when a drug product faces generic competition, the drug is no longer subject to the IRA's price controls. CMS's "bona fide marketing" test obliterates that statutory protection. Under the agency's test, AstraZeneca will have to sell a selected product (including FARXIGA) at the agency's compelled below-market price, despite *also* facing generic competition for that same product, unless and until the agency decides that it is happy with the degree of utilization of the generic drug. That outcome not only flies in the face of the statute's purpose; it also is illogical and fundamentally unfair. It therefore is unlawful under the APA. *See American Fed'n of Gov't Emps., Loc. 2924 v. Federal Lab. Rels. Auth.*, 470 F.3d 375, 380 (D.C. Cir. 2006); *Ponce-Leiva v. Ashcroft*, 331 F.3d 369, 375 (3d Cir. 2003).

III. THE DRUG PRICING PROGRAM VIOLATES DUE PROCESS.

Finally, the IRA's Drug Price Negotiation Program vitiates the Constitution's due-process guarantees. Under the Fifth Amendment, the Government may not deprive a property owner of a property interest without following constitutionally sufficient procedures. U.S. Const. amend. V. Though the Government "may elect not to confer a property interest" at all, "once conferred," the Government "may not

constitutionally authorize the deprivation of" that property interest "without appropriate procedural safeguards." *Cleveland Bd. of Educ. v. Loudermill*, 470 U.S. 532, 541 (1985).

AstraZeneca has protected property interests in its patented drug products and the revenue it derives therefrom. *Horne v. Department of Agric.*, 576 U.S. 351, 359 (2015); *Hartford-Empire Co. v. United States*, 323 U.S. 386, 415 (1945). The IRA deprives AstraZeneca of these property interests by compelling sales of its products at well-below-market prices. 42 U.S.C. § 1320f-3(c)(3)(A). And the law works this deprivation without affording patented property owners like AstraZeneca any procedural safeguards. The statute exempts the agency's deliberation process from public input, insulates from review all critical implementation decisions, and strong-arms manufacturer compliance under threat of unreviewable civil monetary penalties and the so-called excise tax. 42 U.S.C. § 1320f note; *id.* §§ 1320f–6(a), 1320f–7; 26 U.S.C. § 5000D(b). Without ever giving those subject to its mandates an opportunity to be heard, the IRA breezes past the constitutional constraints of due process to achieve one end: drug price restraint at any cost.

On the front end, the IRA forces manufacturers to engage in purported "negotiations" but affords them no leverage, no meaningful opportunity to walk away, and no ability to protect their interests or the interests of the patients who are

ultimately impacted against a so-called "maximum fair price" capped at an amount below actual fair market value.

The IRA mandates implementation of its draconian terms by regulatory fiat, empowering CMS to implement the Drug Price Negotiation Program "for 2026, 2027, and 2028 by program instruction or other forms of program guidance." IRA §§ 11001(c), 11002(c). CMS could have invited public comment before proceeding, just as other agencies have done when enacting congressional directives to set policy through guidance. *See, e.g.*, *Natural Res. Def. Council, Inc. v. EPA*, 22 F.3d 1125, 1131 n.6 (D.C. Cir. 1994) (agency allowed public comment period before implementing statutory directive to publish "guidance for the States"). The agency refused – at least until the program's fourth year.

The IRA also withholds advance notice to AstraZeneca of the forced-sale "agreement," let alone the opportunity to comment or negotiate its contents, 42 U.S.C. §§ 1320f-2(a)(1), 1320f-3(a); the pattern manufacturer "agreement" was not even published *until after* CMS issued its Final Guidance.[5] And "post-promulgation opportunity for comment is not a substitute for pre-promulgation notice and comment." *Universal Health Servs. of McAllen, Inc. v. Sullivan*, 770 F. Supp. 704, 721 (D.D.C. 1991), *aff'd*, 978 F.2d 745 (D.C. Cir. 1992). These front-end infirmities

[5] *See* Ex. 10 (CMS, Medicare Drug Price Negotiation Template), *available at* https://www.cms.gov/files/document/inflation-reduction-act-manufacturer-agreement-template.pdf.

put AstraZeneca at significant risk of being unconstitutionally deprived of its property.

On the back end, the statute purports to block AstraZeneca from seeking judicial review of the most critical implementation decisions, including the agency's "selection of drugs," "the determination of negotiation-eligible drugs," "the determination of qualifying single source drugs," and "[t]he determination of a maximum fair price." 42 U.S.C. § 1320f-7(2)-(3).

In sum, AstraZeneca has no meaningful right to participate or be heard from beginning to end. Looming over this entire scheme are severe (and unreviewable) civil monetary penalties and the so-called excise tax. The IRA also eliminates any exit ramp for manufacturers unwilling to accept below-market prices. Manufacturers can avoid the IRA's negotiation program for a single selected product only by withdrawing the manufacturer's entire portfolio of products from Medicare Part D, but the IRA prevents them from doing so for at least 11 months and as long as 23 months. 42 U.S.C. § 1395w-114a(b)(1)(C)(ii); *id.* § 1395w-114c(b)(4)(B)(ii); *id.* § 1395w-153(a)(1). While CMS has tried to revise this time period downward as a counter to manufacturers' arguments, the statute is plain on this point: A manufacturer's at-will termination of a Medicare agreement can be accomplished no sooner than 11 months after the manufacturer gives notice. *id.* § 1395w-114a(b)(4)(B)(ii)(I). Yet the IRA requires manufacturers to sign "agreements"

accepting below-market prices for selected drugs during that same period – or face ruinous penalties.

Take Farxiga as an example. AstraZeneca is required to sign an Agreement to negotiate with CMS by October 1. Compliance means the signatory will then need to turn over a large volume of highly sensitive commercial information to CMS over the next few months. On March 2, 2024, CMS will proffer a "Maximum Fair Price" that AstraZeneca must respond to. As structured, the IRA leaves AstraZeneca no real choice and no real leverage. The statute creates a sham negotiation process, with no right to judicial review on key issues.

A statutory scheme that forecloses review on the front end and back end, while threatening devastating penalties at every step, violates the precept at the heart of the Due Process Clause: the right of the regulated to an "opportunity to be heard" at "a meaningful time and in a meaningful manner." *Armstrong v. Manzo*, 380 U.S. 545, 552 (1965); *see also Mathews v. Eldridge*, 424 U.S. 319, 335 (1976). The IRA's Drug Price Negotiation Program falls short of that simple command. Because due process demands more, CMS's negotiation program should be invalidated.

CONCLUSION

For all these reasons, the Court should grant AstraZeneca's motion for summary judgment, vacate the Initial Guidance and the Final Guidance, and declare that the IRA Drug Price Negotiation Program violates due process.

Respectfully submitted,

Dated: September 26, 2023

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP and ASTRAZENECA AB, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF HEALTH AND HUMAN SERVICES, and CHIQUITA BROOKS-LASURE, in her official capacity as ADMINISTRATOR OF THE CENTERS FOR MEDICARE & MEDICAID SERVICES, Defendants.	Civil Action No. 23-931-CFC

WORD COUNT CERTIFICATION

Pursuant to the Stipulated Order Regarding Cross-Motions for Summary Judgment (D.I. 15), the undersigned counsel hereby certifies that Plaintiffs' Opening Brief in Support of Plaintiffs' Motion for Summary Judgment was prepared in 14-point Times New Roman font, and contains 7,491 words (excluding the caption, title, tables of contents and authorities, and signature blocks), which were counted using the word count feature in Microsoft Word.

DATED: September 26, 2023

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