IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ASTRAZENECA PHARMACEUTICALS LP, *et al.*, Plaintiffs, v. XAVIER BECERRA, in his official capacity as SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, *et al.*, Defendants.	Civ. No. 1:23-cv-931-CFC

DEFENDANTS' REPLY IN SUPPORT OF MOTION FOR SUMMARY JUDGMENT

BRIAN M. BOYNTON
Principal Deputy Assistant Attorney General

MICHELLE R. BENNETT
Assistant Branch Director

STEPHEN M. PEZZI
Senior Trial Counsel
CHRISTINE L. COOGLE
CASSANDRA M. SNYDER
ALEXANDER V. SVERDLOV
Trial Attorneys

United States Department of Justice
Civil Division, Federal Programs Branch
1100 L Street NW
Washington, D.C. 20005
(202) 451-7729
cassandra.m.snyder@usdoj.gov

Counsel for Defendants

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INTRODUCTION

Plaintiffs' opposition reveals this lawsuit for what it is: a policy dispute that Plaintiffs have recast into a request for an advisory opinion. But Plaintiffs cannot overcome either their lack of Article III standing or Congress's decision to explicitly preclude judicial review over the agency decisions they challenge. Even if they could, Plaintiffs are wrong to think that Congress created two loopholes so big they would swallow much of the Negotiation Program.

First, Plaintiffs have not carried their burden to establish Article III standing on either of their Administrative Procedure Act ("APA") claims. Plaintiffs do not—and cannot—dispute that the two challenged aspects of the Revised Guidance had no effect on the selection of Plaintiffs' drug Farxiga for the 2026 program cycle. Instead, Plaintiffs complain of self-inflicted injuries based on speculative assumptions about how possible future guidance *might* cause them some future harm. Article III does not countenance Plaintiffs' request for an advisory opinion to wield against hypothetical future guidance.

Second, Plaintiffs' APA claims are straightforwardly precluded by the plain text of the Inflation Reduction Act ("IRA"). Congress provided that "[t]here shall be no administrative or judicial review" of certain agency decisions, including the "selection of drugs" for negotiation, the "determination of negotiation-eligible drugs," and the "determination of qualifying single source drugs." 42 U.S.C. § 1320f-7. Yet Plaintiffs challenge the methods by which the Centers for Medicare & Medicaid Services ("CMS") makes the very determinations over which Congress expressly precluded review. Under the plain text of the statute and settled precedent interpreting similar preclusion

provisions—which are common in the Medicare context—this Court lacks jurisdiction over Plaintiffs' APA claims.

In any event, Plaintiffs' APA claims fail on the merits. Both challenges are premised on imagined loopholes that contradict clear statutory language. Plaintiffs' interpretation of "qualifying single source drug" would allow manufacturers to end-run the Negotiation Program based on how they choose to vary their drug products and seek Food and Drug Administration ("FDA") approval. And Plaintiffs' definition of "is … marketed" would render that phrase almost meaningless.

Finally, Plaintiffs' due process claim is meritless for reasons explained in *Dayton Area Chamber of Commerce v. Becerra*, No. 3:23-cv-156, --- F. Supp. 3d ---, 2023 WL 6378423 (S.D. Ohio Sept. 29, 2023) (*Chamber*). In short, "[t]he law established" around the country "is clear: participation in Medicare, no matter how vital it may be to a business model, is a completely voluntary choice." *Id.* at *11. There is thus no deprivation of a protected property interest in violation of the Due Process Clause, "because pharmaceutical manufacturers who do not wish to participate in the Program have the ability—practical or not—to opt out of Medicare entirely." *Id.*

The Court should dismiss Plaintiffs' APA claims for lack of jurisdiction and enter judgment for Defendants on Plaintiffs' due process claim.

ARGUMENT

I. Plaintiffs lack Article III standing to bring their APA claims.

Plaintiffs do not dispute that "the program guidance that Plaintiffs challenge governs only the first negotiation cycle." Defs.' MSJ at 2, ECF No. 21-1; *accord* Decl. of Cheri Rice ¶ 12, ECF No. 21-2 ("Rice Decl."). Nor do Plaintiffs dispute that, "even

if CMS had made *both* of Plaintiffs' preferred interpretive choices" in that guidance, "that would have had no effect on the inclusion of AstraZeneca's drug Farxiga among the drugs CMS selected for negotiation." Defs.' MSJ at 2; *accord* Rice Decl. ¶ 8. Those undisputed propositions are fatal to Plaintiffs' standing to bring their APA claims. In response, Plaintiffs now turn to speculation about possible future injuries caused by possible future guidance. But Article III prohibits advisory opinions premised on such a "hypothetical" state of facts. *TransUnion LLC v. Ramirez*, 594 U.S. 413, 424 (2021); *see also, e.g.*, *Rhone-Poulenc Surfactants & Specialties, L.P. v. Comm'r of Int'l Revenue*, 249 F.3d 175, 182 (3d Cir. 2001) (refusing to give advisory opinion on hypothetical factual scenario).

A. Plaintiffs cannot manufacture injury based on hypothetical future events.

An injury-in-fact must be "'certainly impending," not merely "a 'possible future injury.'" *Clemens v. ExecuPharm Inc.*, 48 F.4th 146, 152–53 (3d Cir. 2022) (citation omitted). But Plaintiffs' purported injuries are all based on a series of unsupported assumptions about hypothetical future events.

1. Plaintiffs first assert that the Revised Guidance's definition of "qualifying single source drug" will decrease Plaintiffs' incentives to "innovate new uses for Farxiga's single-ingredient active moiety." Pls.' Opp. at 7, ECF No. 58. But Plaintiffs cannot "manufacture standing merely by inflicting harm on themselves based on their fears of hypothetical future harm that is not certainly impending." *Clapper v. Amnesty Int'l USA*, 568 U.S. 398, 416 (2013); *see also, e.g.*, *Parker v. Governor of Pa.*, No. 20-3518, 2021 WL 5492803, at *2–3 (3d Cir. Nov. 23, 2021).

Any choice by Plaintiffs to not seek "new uses" for their existing drug is premised on speculation that, if they develop any new formulation, that formulation will be subject to the same maximum fair price ("MFP") negotiated for Farxiga. Pls.' Opp. at 7. But Plaintiffs fail to establish the likelihood of either link in this "speculative chain of future events." *Reilly v. Ceridian Corp.*, 664 F.3d 38, 46 (3d Cir. 2011); *see id.* at 43 ("[O]ne cannot describe how [plaintiffs] will be injured without beginning the explanation with the word 'if.'" (citation omitted)). First, Plaintiffs have not established that they will imminently develop another formulation with Farxiga's active moiety. In fact, Plaintiffs explicitly *concede* that they are not undertaking any clinical trials that could have such a result. *See* Pls.' Opp. at 8; Decl. of Jim Ader ¶ 23, ECF No. 60 ("Ader Decl."). To resuscitate their hypothetical injury, Plaintiffs refer vaguely to "ongoing drug development efforts" involving Farxiga's active moiety. *See* Pls.' Opp. at 8. But a hypothetical impediment to undefined, non-clinical "development efforts," *id.*, is not a "certainly impending" injury, *Clapper*, 568 U.S. at 409–10. Indeed, Plaintiffs themselves emphasize that "[i]t can take decades … to shepherd a single potential new therapy through clinical trials," and only 0.02% of compounds that enter preclinical testing ultimately achieve FDA approval. *See* Ader Decl. ¶ 7; *see also* Pls.' Opp. at 2 ("Even when a drug shows early promise in clinical trials, the rigorous drug approval process means very few of these research efforts result in a new drug or indication.").

Second, even crediting Plaintiffs' speculation that they may one day obtain FDA approval for some hypothetical new formulation with Farxiga's active moiety, Plaintiffs' theory of financial disincentive rests entirely on their unsupported assumption that Farxiga will be a selected drug with an MFP at that (unknown) time. But that is

especially unlikely given Plaintiffs' assertion that "17 generic manufacturers" are already tentatively approved "to market generic versions of FARXIGA." Pls.' Opp. at 9; *see also* 42 U.S.C. § 1320f-1(e)(1)(A)(iii) (a drug is not a "qualifying single source drug" if a generic version of that drug "is … marketed"); *but see* 21 C.F.R. § 314.3(b) (a tentative approval does not become a full approval unless and "until FDA issues an approval letter after any necessary additional review of the NDA or ANDA"). If Farxiga were de-selected due to the marketing of an approved generic competitor, as Plaintiffs predict, then Plaintiffs would have no basis to fear that any speculative new drug product would be subject to a negotiated MFP for Farxiga.

2. Plaintiffs similarly assert that the Revised Guidance will have unspecified effects on Plaintiffs' "decision-making about other drugs" besides Farxiga. Pls.' Opp. at 11. But such "vague," "generalized" assertions fail to establish a cognizable injury. *Nat'l Shooting Sports Found. v. Att'y Gen. of N.J.*, 80 F.4th 215, 220 (3d Cir. 2023) (declarations asserting unspecified, vague chilling effect did not establish injury). Plaintiffs' assertions that they have "been forced to make decisions now based on the agency policies currently in place," Ader Decl. ¶¶ 31–32; *see* Pls.' Opp. at 11, lack any specificity as to what "decision-making" has been affected, or how.

Moreover, Plaintiffs' future "decision-making" about other drugs is, again, necessarily premised on a "highly attenuated chain" of hypothetical future events. *Clapper*, 568 U.S. at 410. First, Plaintiffs cannot establish that any particular drug will be selected in future program cycles based on speculation about what future guidance may provide. *See infra* pp. 8–9; Defs.' MSJ at 18; *see also Sabre, Inc. v. Dep't of Transp.*, 429 F.3d 1113, 1117 (D.C. Cir. 2005) (plaintiff had standing where agency "indicate[d] a

very high probability that it [would] act against a practice" which the plaintiff had shown detailed evidence of its desire to pursue); *Carbon Sequestration Council v. EPA*, 787 F.3d 1129, 1141–42 (D.C. Cir. 2015) (contrasting the plaintiff's "speculative concern that EPA may choose to regulate its business at some point in the indefinite future" against *Sabre*).

Second, whether or not future guidance is similar to current guidance, Plaintiffs' drugs may be selected even under *Plaintiffs'* interpretation of the IRA. For example, Plaintiffs complain that the Revised Guidance would render the new "tablet form" of Plaintiffs' drug Lynparza eligible for selection immediately, because the former "capsule form" of Lynparza is already eligible for selection. *See* Pls.' Opp. at 12–13. But the tablet form of Lynparza would meet the temporal requirement for selection for the next program cycle even under *Plaintiffs'* theory. *See* FDA, NDA Approval for Lynparza Tablets (Aug. 17, 2017), https://perma.cc/H5UJ-C2PR (approving tablet form on August 17, 2017); 42 U.S.C. § 1320f(b)(3) (setting next selected drug publication date as February 1, 2025—more than seven years after FDA approved Lynparza's tablet form). Plaintiffs similarly fail to establish that Calquence will be selected before August 4, 2029—*i.e.*, seven years after FDA approved Calquence's tablet form. *See* FDA, NDA Approval for Calquence Tablets (Aug. 4, 2022), https://perma.cc/XEB4-EVVC; 42 U.S.C. § 1320f-1(e)(1)(A)(ii).

3. Plaintiffs separately assert that the Revised Guidance's bona fide marketing standard will "subject" Farxiga "to generic competition *and* mandatory

pricing" when generics for Farxiga enter the marketplace in the future. Pls.' Opp. at 9.[1] But to establish that the bona fide marketing standard will harm Plaintiffs under this theory, Plaintiffs must establish that there will be generics for Farxiga that will be marketed at only a *de minimis* level—*i.e.*, generics that are "marketed" in some non-zero amount, but that do not rise to the level of "bona fide marketing." *See* Defs.' MSJ at 17; 42 U.S.C. § 1320f-1(e)(1)(A)(iii). Plaintiffs themselves confirm how unlikely that is, predicting that as many as *seventeen* generics for Farxiga may be entering the market in 2025 and 2026. *See* Pls.' Opp. at 8; Ader Decl. ¶ 27. Thus—even assuming (as Plaintiffs do) that those generics obtain FDA approval and enter the market—Plaintiffs would have to establish that *all seventeen* of these generics would be marketed at only a *de minimis* level in order for Plaintiffs' subtle disagreement with CMS to matter. Plaintiffs cannot do so.

Finally, Plaintiffs speculate that alleged "delay[]" in Prescription Drug Event ("PDE") data will result in CMS delaying de-selection of Farxiga following entry of a bona-fide-marketed generic. Pls.' Opp. at 9. But Defendants have already explained that CMS will also consider average manufacturer price ("AMP") data and "'multiple' other sources" to bridge any delays in PDE data. Defs.' MSJ at 42 (citing *Medicare Drug Price Negotiation Program: Revised Guidance* at 77, 165, 170 (June 30, 2023), https://perma.cc/K6QBC3MM ("Revised Guidance"). Plaintiffs make no attempt to

[1] Because "'standing is not dispensed in gross,' a plaintiff who raises multiple causes of action 'must demonstrate standing for each claim he seeks to press.'" *In re Schering Plough Corp.*, 678 F.3d 235, 245 (3d Cir. 2012) (citation omitted). Plaintiffs' assertions of injury related to the bona fide marketing standard thus cannot establish standing related to the definition of "qualifying single source drug," or vice versa.

establish that these additional data sources are "delayed," instead merely speculating—without any evidence—that Farxiga's de-selection would be delayed upon entry of a bona-fide-marketed generic. Moreover, Plaintiffs can also only speculate that any such hypothetical delay would injure them. Even if Farxiga's hypothetical de-selection were delayed, such delay may not affect prices of Farxiga depending on when the delay occurred. *See* Revised Guidance at 92, 166.

B. Plaintiffs cannot establish causation or redressability based on future guidance.

Plaintiffs' summary treatment of causation and redressability ignores that the Revised Guidance applies only to program year 2026 and thus cannot cause any injury in future program cycles. *See* Defs.' MSJ at 18. And Plaintiffs' "self-inflicted injuries" based on speculative assumptions of what *future* guidance might look like "are not fairly traceable" to any actual, existing agency action. *Clapper*, 568 U.S. at 418.

Plaintiffs now confirm that their APA claims are premised on the unexplained and unsupported assumption that future guidance will be identical to the current guidance. *See* Pls.' Opp. at 13–14; Ader Decl. ¶¶ 31–32. Yet even if that assumption holds, it would still not be the *current* guidance that injures Plaintiffs—it would be some (currently hypothetical) *future* guidance. Of course, if Plaintiffs suffer some actual or imminent injury in future negotiation cycles, they can then challenge that future guidance. But Plaintiffs cannot challenge the current guidance—which has no legal effect on future negotiation cycles, *see* Revised Guidance at 1–2; Rice Decl. ¶ 12—in the hope of obtaining a preemptive court order to wield against hypothetical future guidance, *see, e.g.*, *Miller v. FCC*, 66 F.3d 1140, 1145 (11th Cir. 1995).

For similar reasons, an order setting aside the Revised Guidance would not redress Plaintiffs' alleged injuries. Plaintiffs seek "certainty" about the definition of "qualifying single source drug" in future guidance. Pls.' Opp. at 16. But an order setting aside the Revised Guidance for program year 2026 would set aside only the Revised Guidance for program year 2026. And any persuasive effect of such an order is irrelevant to Article III standing. After all, "[r]edressability requires that the court be able to afford relief *through the exercise of its power*, not through the persuasive or even awe-inspiring effect of the opinion *explaining* the exercise of its power." *Haaland v. Brackeen*, 599 U.S. 255, 294 (2023) (quoting *Franklin v. Massachusetts*, 505 U.S. 788, 825 (1992)). Plaintiffs' desire for "certainty" about currently non-existent guidance does not entitle them to an advisory opinion. *See TransUnion LLC*, 594 U.S. at 422–23; *Preiser v. Newkirk*, 422 U.S. 395, 401 (1975).

II. Congress expressly precluded judicial review of Plaintiffs' APA claims.

The IRA precludes review of CMS's "selection of drugs" for negotiation under section 1320f-1(b), CMS's "determination of negotiation-eligible drugs" under section 1320f-1(d), and CMS's "determination of qualifying single source drugs" under section 1320f-1(e). 42 U.S.C. § 1320f-7(2). This plain language expressly precludes Plaintiffs' challenges to the methods by which CMS makes those selections and determinations, which are necessarily challenges to CMS's selections and determinations themselves. Moreover, the methods of selection are clearly "indispensable," "'integral' to," and "'inextricably intertwined' with" the selections themselves, and are therefore also expressly precluded on those grounds. *Fla. Health Scis. Ctr. v. Sec'y of HHS*, 830 F.3d 515, 519 (D.C. Cir. 2016) (quoting *Tex. All. for Home Care Servs. v. Sebelius*, 681 F.3d 402,

409–11 (D.C. Cir. 2012)). None of Plaintiffs' efforts to evade this conclusion find footing.

A. Plaintiffs first seek to evade the IRA's plain language by claiming that they do not challenge CMS's "identification of particular drugs." Pls.' Opp. at 19. It is hard to see how that is so. Plaintiffs challenge the definition of qualifying single source drug and the bona fide marketing standard *because* they may require the selection of Plaintiffs' drugs under sections 1320f-1(b), (d), and (e). Indeed, the crux of Plaintiffs' standing theory is that these methods for selecting drugs will harm Plaintiffs by mandating the selection of Plaintiffs' drugs (as drugs selected for negotiation, negotiation-eligible drugs, and qualifying single source drugs) in the future. *See, e.g.*, Pls.' Opp. at 6–8 (alleging injury because any future formulation with Farxiga's active moiety would be selected "as the same Qualifying Single Source Drug as FARXIGA"); *id.* at 8–10 (alleging injury because "CMS might improperly keep FARXIGA on the selected drug list"); *id.* at 11 (alleging injury because "AstraZeneca will very likely have products on [the] list" for future program cycles). Plaintiffs therefore plainly challenge CMS's methods because the methods allegedly involve CMS's future determination of particular drugs.

Plaintiffs attempt to skirt this conclusion by arguing that the challenged methods and the precluded determinations are distinct, simply because the challenged methods are "relevant" to other provisions of the Negotiation Program besides the selection of drugs for negotiation, the determination of negotiation-eligible drugs, and the determination of qualifying single source drugs. Pls.' Opp. at 19–20. But the mere fact that the terms "qualifying single source drug" and "marketed" appear in other

provisions of the IRA—and thus may have bearing on other aspects of the Program—does not allow Plaintiffs to evade an express preclusion provision. To the contrary, courts have held that similar preclusion provisions cover decisions that are "'indispensable' or 'integral' to, or 'inextricably intertwined' with, the unreviewable agency action," even if those decisions may have bearing on some other elements of an agency's activity. *Fla. Health Scis. Ctr.*, 830 F.3d at 519 (citation omitted); *see* Defs.' MSJ at 25 (collecting cases). And courts consider a decision to be "expressly" precluded from review where it is "'inextricably intertwined' with[] the unreviewable agency action." *Id.*[2]

Plaintiffs' own cited cases embrace this standard. In both *American Clinical Laboratory Association v. Azar*, 931 F.3d 1195 (D.C. Cir. 2019), and *Baxter Healthcare Corp. v. Weeks*, 643 F. Supp. 2d 111 (D.D.C. 2009), the challenged agency determinations arose under legal obligations that were genuinely distinct from the unreviewable agency actions. In *American Clinical*, the challenged determination was not "inextricably intertwined with" the unreviewable agency action because it arose under a "distinct" statutory provision that imposed "new obligations" and even included a discrete notice-and-comment requirement. 931 F.3d at 1205–07. The unreviewable action therefore "[did] not *subsume* the" challenged determination. *Id.* at 1206 (emphasis added). The

[2] Plaintiffs assert that finding preclusion here would transform the preclusion provision into a "sweeping bar to judicial review of *any* aspects of the" Negotiation Program. Pls.' Opp. at 20. Not so. Among other reasons, Defendants have expressly disclaimed any application of the preclusion provision to Plaintiffs' due process challenge. *See* Defs.' MSJ at 22. And to date, the government has not raised the preclusion bar in any of the six other lawsuits challenging this program in which the government has filed briefing. *See id.* at 13 (collecting cases).

D.C. Circuit expressly distinguished the case from *Florida Health, Texas Alliance*, and *Mercy Hospital*, which—like here—did not involve distinct legal obligations. *See id.* at 1206–07. Similarly, in *Baxter Healthcare*, the challenged determination was made under a separate provision with its own detailed obligations, distinct from the unreviewable agency action. 643 F. Supp. 2d at 115.

Here, the challenged methods do not arise under a legal framework distinct from CMS's selection of drugs, determination of negotiation-eligible drugs, or determination of qualifying single source drugs. Rather, CMS's selection of drugs necessarily "subsume[s]" the methods by which CMS selects those drugs. *American Clinical*, 931 F.3d at 1206. Plaintiffs thus seek to "do[] exactly what the plaintiffs in *Florida Health* and *DCH Regional* did: complain[] about the method that was used" to make a determination that Congress exempted from review. *Scranton Quincy Hosp. Co. v. Azar*, 514 F. Supp. 3d 249, 262 (D.D.C. 2021).

Plaintiffs also mischaracterize the holding of *American Hospital Association v. Azar*, 964 F.3d 1230 (D.C. Cir. 2020), as broadly allowing a plaintiff to bypass a preclusion provision when the plaintiff alleges *any* violation of statutory authority, *see* Pls.' Opp. at 22. Plaintiffs' reading of *American Hospital* would swallow the ultra vires doctrine, which (at most) allows claims to proceed past a preclusion provision only if—among other requirements—a plaintiff alleges an "extreme" statutory violation. *DCH Reg'l Med. Ctr. v. Azar*, 925 F.3d 503, 509 (D.C. Cir. 2019); *see also infra* pp. 14–15 (discussing ultra vires requirements). Rather, *American Hospital* dealt with a unique preclusion provision barring only certain statutorily authorized "methods," which rendered it "effectively coextensive" with the plaintiff's statutory-authorization claim. 964 F.3d at 1238–39.

Thus, to determine whether that provision barred review of the challenged determination, the court was forced to first determine whether the challenged determination was statutorily authorized. *See id.* Unlike that provision, the IRA's preclusion provision does not preclude review only of certain statutorily authorized methods. The IRA precludes *all* review of CMS's selection of drugs under sections 1320f-1(b), (d), and (e)—which necessarily includes the methods by which CMS selects drugs under those same sections.

Plaintiffs fail to distinguish the many cases, *see* Defs.' MSJ at 24–25, in which a preclusion provision barred a decision that was "'indispensable' or 'integral' to, or 'inextricably intertwined' with, the unreviewable agency action," *Fla. Health Scis. Ctr.*, 830 F.3d at 519 (citation omitted). For example, Plaintiffs do not even attempt to reconcile their position with the D.C. Circuit's conclusion that a "distinction between methodology and estimates would eviscerate the statutory bar" against review, "for almost any challenge to an estimate could be recast as a challenge to its underlying methodology." *DCH Reg'l*, 925 F.3d at 506. Plaintiffs argue only that these cases involved "pure arbitrary-and-capricious challenge[s]." Pls.' Opp. at 23. Plaintiffs do not explain why the particular type of APA claim matters for preclusion purposes. The IRA's preclusion provision bars all "administrative or judicial review" of the specified actions, not just review of arbitrary-and-capricious challenges. 42 U.S.C. § 1320f-7. In any event, Plaintiffs are wrong: many of Defendants' cited cases involved challenges to the agencies' statutory authority, not simply arbitrary-and-capricious challenges. *See, e.g.*, *Tex. All. for Home Care Servs. v. Sebelius*, 811 F. Supp. 2d 76, 98 (D.D.C. 2011) (ultra vires violation), *aff'd*, 681 F.3d 402 (D.C. Cir. 2012); *Knapp Med. Ctr. v. Burwell*, 192 F.

Supp. 3d 129, 133 (D.D.C. 2016) (statutory violation), *aff'd sub nom. Knapp Med. Ctr. v. Hargan*, 875 F.3d 1125 (D.C. Cir. 2017). The reasoning of those cases applies here too. And of course, Plaintiffs here *also* bring arbitrary-and-capricious claims.

B. Plaintiffs' resort to the ultra vires doctrine fares no better. Having failed to present this claim in their complaints or opening papers, Plaintiffs seek to raise a new ultra vires claim for the first time in their opposition to Defendants' summary-judgment motion. But even accepting that the APA "authorize[s]" an ultra vires claim, Pls.' Opp. at 25, that does not relieve Plaintiffs from properly pleading it, *see, e.g.*, *Waugaman v. City of Greensburg*, 841 F. App'x 429, 433 (3d Cir. 2021) ("[A] 'plaintiff may not amend his complaint through arguments in his brief in opposition to a motion for summary judgment.'" (quoting *Shanahan v. City of Chi.*, 82 F.3d 776, 781 (7th Cir. 1996))).

Regardless, even if they amended their complaint (again), Plaintiffs cannot meet the requirements for an ultra vires claim. *See* Defs.' MSJ at 26 n.6. First, it is plainly not the case that "the statutory preclusion of review is implied rather than express." *DCH Reg'l*, 925 F.3d at 509. The IRA expressly precludes judicial review of CMS's selection and determination of drugs under sections 1320f-1(b), (d), and (e), and the methods by which CMS does so. *See* 42 U.S.C. § 1320f-7(2). *American Hospital Association v. Becerra*, 596 U.S. 724, 733 (2022), does not establish otherwise. There, the court simply confirmed that a provision precluding review of one payment method did not implicitly bar review of an entirely separate and statutorily distinct payment method. *See id.* And, as explained, courts consider preclusion provisions to "express[ly]" bar review of determinations that are—as here—"'indispensable,'" "'integral' to," and

"'inextricably intertwined' with" the precluded determinations. *DCH Reg'l*, 925 F.3d at 509, 519; *see also Fla. Health Scis. Ctr.*, 830 F.3d at 519; *Tex. All.*, 681 F.3d at 404.

Second, Plaintiffs' claims (even if they had merit) do not establish "'extreme' agency error." *DCH Reg'l*, 925 F.3d at 509. Such extreme error is implicated only when "the agency plainly acts … *contrary to a specific prohibition in the statute that is clear and mandatory*.'" *Id.* (emphasis added); *see also Nyunt v. Chairman, Broad. Bd. of Governors*, 589 F.3d 445, 449 (D.C. Cir. 2009) (Kavanaugh, J.) (an ultra vires claim is "a Hail Mary Pass" that "rarely succeeds"). Plaintiffs identify no such prohibition. *See, e.g.*, *Fla. Health Scis. Ctr.*, 830 F.3d at 522–23 (rejecting plaintiff's attempt "to 'couch[]' this type of reasonableness challenge 'in terms of the agency's exceeding its statutorily-defined authority" (quoting *Nw. Airlines, Inc. v. FAA*, 14 F.3d 64, 73 (D.C. Cir. 1994))). Nor does a claim implicate extreme error simply because the underlying statute and implementing regulations may be "historic," Pls.' Opp. at 26—a label that has no bearing on whether the agency committed an "obvious violation of a clear statutory command," *DCH Reg'l*, 925 F.3d at 509, and that would create a new and undefined substantive canon out of thin air.

III. Plaintiffs' APA claims are meritless.

Even setting aside the threshold jurisdictional defects barring Plaintiffs' APA challenges, those claims would also fail on the merits.

A. CMS's approach to multiple forms of the same drug is consistent with the IRA.

The Revised Guidance interprets the IRA's plain text to require consideration of all "dosage forms and strengths" of a drug with the same active moiety. 42 U.S.C.

§ 1320f-1(d)(3)(B); *id.* § 1320f-5(a)(2). By contrast, Plaintiffs' interpretation of "qualifying single source drug" would require CMS to consider all "dosage forms and strengths" of a drug with the same active moiety, *except* when the different dosage form or strength was approved under a different NDA. *See* Pls.' Opp. at 30. There is no basis for this atextual exception.

As Defendants explained, *manufacturers* may, in certain instances, choose whether to submit either a new NDA or a supplemental NDA ("sNDA") for a new drug product with the same active moiety as a drug product approved under an existing NDA. *See* Defs.' MSJ at 15; 21 C.F.R. § 314.3(b) (defining "drug product" as "a finished dosage form, e.g., tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients"). As a result, FDA often approves multiple drug products under the same NDA. *See, e.g.*, Pls.' Opp., Ex. 1, FDA, *Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees* 3–4 (2004) (describing circumstances for submitting different drug products under a single NDA), ECF No. 59-1. Plaintiffs resist this conclusion, citing 21 U.S.C. § 355(b)(4) to suggest that manufacturers lack *any* choice in whether to submit an NDA or an sNDA.[3] *See* Pls.' Opp. at 7 n.3. But section 355(b)(4) restricts a manufacturer's ability to amend or supplement an NDA for a "different drug," not a "different drug product," and only for a certain subset of NDAs (those submitted under section 355(b)(2)). In fact, a manufacturer *may*, in certain instances, choose whether to pursue approval for a new drug product under a new NDA or an sNDA. And it would

[3] Plaintiffs' citation to "21 U.S.C. § 355(c)(4)" is presumably intended to be section 355(b)(4). Pls.' Opp. at 7 n.3. Section 355(c)(4) has no relevance here.

make little sense for Congress to subject the Negotiation Program to the strategic whims of the manufacturers themselves, who could attempt to evade the Program by submitting new applications rather than supplemental applications.

Plaintiffs' own brief neatly illustrates the nonsensical result of Plaintiffs' interpretation. Plaintiffs complain that the original "capsule form" and the new "tablet form" of their drug Lynparza—which contain the same active moiety but which were approved under distinct NDAs—would unfairly count as the same "qualifying single source drug" under the Revised Guidance. Pls.' Opp. at 12; *see also id.* at 13 (same regarding Calquence). But the IRA expressly directs CMS to consider "data that is aggregated across dosage forms and strengths of the drug, including new formulations of the drug"—such as a new "tablet" dosage form, Pls.' Opp. at 12—when determining whether a qualifying single source drug is negotiation-eligible, *see* 42 U.S.C. § 1320f-1(d)(3)(B). And the IRA also expressly directs CMS to "apply the [MFP] across different strengths and dosage forms of a selected drug and not based on the specific formulation or package size or package type of such drug." *Id.* § 1320f-5(a)(2). Plaintiffs' attempt to artificially exclude a new "dosage form[]" of a drug just because it was approved pursuant to a new NDA is contrary to these explicit statutory mandates. Indeed, Plaintiffs' suggestion that the capsule and the tablet forms of Lynparza (and of Calquence) should not be treated as the same "qualifying single source drug" lays bare Plaintiffs' desire to game the IRA and get out from under the choices Congress made. The IRA would be significantly hobbled if a manufacturer could avoid selection eligibility by shifting sales from an eligible drug product to a new tablet form of the same drug, contrary to congressional intent.

Plaintiffs' resort to a series of attenuated cross-references, *see* Pls.' Opp. at 29, fails to overcome the IRA's express language. The IRA cross-references the definition of a "covered part D drug" in section 1395w-102(e) merely to ensure that a qualifying single source drug is a drug eligible for reimbursement under Medicare Part D. The definition of a "covered part D drug," in turn, cross-references the general Medicaid definition of a "covered outpatient drug" in section 1396r-8(k)(2), which unsurprisingly requires that a drug be FDA-approved to be eligible for Medicaid reimbursement. These definitions do not mean, explicitly or implicitly, that FDA approval creates a distinct, *new* "covered outpatient drug." Indeed, contrary to Plaintiffs' characterization, *see* Pls.' Opp. at 29, a district court in *Ipsen Biopharmaceuticals, Inc. v. Azar* recently held that a new NDA alone does *not* suffice to establish a "new 'covered outpatient drug'" for Medicaid-rebate purposes. No. 16-cv-2372, 2020 WL 3402344, at *10 (D.D.C. June 19, 2020) (agreeing with government's position that "a new NDA (absent changes to the drug's dosage form or strength) is necessary, *but not always sufficient*, to establish new base date information for Medicaid rebate purposes").

B. CMS properly explained its approach.

Plaintiffs fare no better with their arbitrary-and-capricious challenge. "Judicial review under [the arbitrary-and-capricious standard] is deferential," *FCC v. Prometheus Radio Project*, 592 U.S. 414, 423 (2021), and "presume[s] the validity of agency action," *SBC Inc. v. FCC*, 414 F.3d 486, 496 (3d Cir. 2005) (citation omitted); *see also Citizens to Pres. Overton Park, Inc. v. Volpe*, 401 U.S. 402 (1971).

In the face of that deferential standard, Plaintiffs repeat generalized complaints that CMS's definition of "qualifying single source drug" might disincentivize

innovation. But Plaintiffs are entirely silent on Defendants' lengthy responsive discussion of "product hopping." *See* Defs.' MSJ at 31–32. Plaintiffs ignore that manufacturers can improperly maintain high prices by introducing inconsequential changes to their drugs and shifting patients to the new versions, and that such product hopping can itself *reduce* innovation. *See id.* at 32. Plaintiffs ignore that considering all dosage forms and strengths of a drug—consistent with the statutory language—decreases incentives to product hop. *See id.* at 31. And Plaintiffs' failure to refute any desire to engage in product hopping—at the expense of Medicare beneficiaries and American taxpayers—is telling.

Plaintiffs assert that CMS "failed to consider an important aspect of the problem," Pls.' Opp. at 34, but they have not identified a single issue that CMS did not already explicitly address in the Revised Guidance. Plaintiffs fail to engage with any of CMS's explanations. For example, Plaintiffs attach a comment on the Initial Guidance regarding alleged hindrance to innovation for "ultra-rare uses of existing treatments." Pls.' Ex. 9 at 64, ECF No. 59-1; *see* Pls.' Opp. at 33. But Plaintiffs do not engage at all with Defendants' explanation—as laid out in the Revised Guidance—that CMS will take medical impact into account in negotiating prices. *See* Defs.' MSJ at 32; *see also* Revised Guidance at 12, 147–51. Plaintiffs' generalized assertions regarding CMS's definition of "qualifying single source drug" fall far short of overcoming the deferential arbitrary-and-capricious standard.

C. CMS's bona fide marketing standard is consistent with the IRA.

The Revised Guidance explains that a generic drug or biosimilar "is … marketed" for the purposes of the IRA, 42 U.S.C. § 1320f-1(e)(1)(A)(iii), (B)(iii), "when

the totality of the circumstances … reveals that the manufacturer of that drug or product is engaging in *bona fide* marketing of that drug or product." Revised Guidance at 102 (emphasis added). This common-sense approach confirms that a generic drug or biosimilar is subject to "meaningful competition" before a selected drug is removed from the Negotiation Program. *Id.* at 74. It therefore addresses circumstances in which brand-name manufacturers enter into "market-limiting agreement[s]" with a generic manufacturer, under which the generic manufacturer "agrees to limit production or distribution of the generic version of the drug, such that only a nominal quantity of product is allowed to enter the market." *Id.* Plaintiffs attempt to avoid the requirement that "market[ing]" be meaningful, and not merely *de minimis*, by creating a loophole in the IRA. None of Plaintiffs' arguments override the IRA's clear statutory language.

First, even Plaintiffs' own purported "ordinary meaning" of the term "marketed," *see* Pls.' Opp. at 37, is consistent with the Revised Guidance. Nothing in that definition—to "expose[] … for sale in a market"—forecloses CMS from considering whether a generic drug was *meaningfully* "expose[d] … for sale in a market."[4] *Id.* at 38. On its face, the phrase "is … marketed" reflects actual and ongoing commercial activity—not a mere token presence. This is especially so given Congress's express delegation of authority to CMS to "determine[]," through unspecified procedures, whether a generic drug "is marketed." 42 U.S.C. § 1320f-1(c)(1)(B); *see*

[4] In an analogous context, Plaintiffs themselves recently argued that the term "offer" in the 340B statute, 42 U.S.C. § 256b(a)(1), necessarily implies "bona fide." *See* Br. for Appellee AstraZeneca Pharma. LP at 23, 43, No. 22-1676 (3d Cir. July 21, 2022); *see also* Br. for Appellee Novartis Pharma. Corp. at 39, No. 21-5299 (D.C. Cir. June 8, 2022) ("Of course, manufacturers' offers must still be 'meaningful' and 'bona fide[.]'").

Defs.' MSJ at 34–35. Plaintiffs offer no response to case law explaining that the phrase "as determined by the Secretary" is an "express delegation of authority" to exercise "discretion." *Transitional Hosps. Corp. of La. v. Shalala*, 222 F.3d 1019, 1025 (D.C. Cir. 2000) (citation omitted); Defs.' MSJ at 24–35. If Congress had truly intended CMS to conduct a check-the-box inquiry, Congress could have directed CMS to consider a database such as the FDA's National Drug Code Directory, as Congress did elsewhere in the IRA in 42 U.S.C. § 1395w-114b(g)(1)(C)(ii). *See* Defs.' MSJ at 35. Plaintiffs' sole argument against CMS's authority to conduct ongoing monitoring is that Congress "could have" used stronger language. Pls.' Opp. at 41. But Plaintiffs ignore Congress's intentional choice of verb tense. *See* Defs.' MSJ at 36 (citing *Carr v. United States*, 560 U.S. 438, 448 (2010)). The IRA specifically refers to a drug that "*is* marketed," not a drug that "was marketed" or "has been marketed." *See* 42 U.S.C. § 1320f-1(e)(1) (emphasis added). Congress was not required to belabor the point.

Plaintiffs' citations to other authorities have no bearing on the IRA. Plaintiffs do not dispute that their cited authorities did not arise "in a context where *de minimis* marketing would plausibly be a concern." Pls.' Opp. at 38 (quoting Defs.' MSJ at 38). Despite this concession, Plaintiffs argue that Congress would have "added qualifying language" if Congress intended to impose a different definition. *Id.* at 39. But when two uses of a term are concededly not comparable, Congress has no need to "add[] qualifying language." *Id.*; *see Env't Def. v. Duke Energy Corp.*, 549 U.S. 561, 574 (2007).

Having previously relied heavily on *Asgrow Seed Co. v. Winterboer*, 513 U.S. 179, 186 (1995), Plaintiffs now reduce discussion of that case to a footnote, *see* Pls.' Opp. at 39 n.13—conflating the Revised Guidance's "bona fide marketing" standard with the

"extensive" marketing standard rejected in *Asgrow*. But while "bona fide marketing" merely excludes *de minimis* activities, the "extensive" marketing standard rejected in *Asgrow* required "extensive or coordinated selling activities." *Id.* at 187. *Asgrow* did not consider whether "marketing" encompassed *de minimis* marketing, because there was no dispute in that case that the defendants were engaged in a bona fide effort to sell the product at issue. And contrary to Plaintiffs' assertion that it is "irrelevant" that *Asgrow* involved interpretation of an entirely different statute, *see* Pls.' Opp. at 39 n.13, the Supreme Court expressly relied on the specific context of "the law at issue" in conducting its statutory interpretation, *see Asgrow*, 513 U.S. at 187.

Ultimately, Plaintiffs do not even dispute that the imagined loophole at the center of their "interpretation of the IRA 'would flout Congress's purpose.'" *See* Pls.' Opp. at 41. Plaintiffs fail to establish that the bona fide marketing standard contradicts the IRA, especially given that Congress did not intend to enact a toothless "marketing" standard. *See Panzarella v. Navient Sols., Inc.*, 37 F.4th 867, 872–73 (3d Cir. 2022) ("As '[s]tatutory language cannot be construed in a vacuum,' we turn next to [the term's] context." (quoting *Weyerhaeuser Co. v. U.S. Fish & Wildlife Serv.*, 139 S. Ct. 361, 367 (2018))). "That [P]laintiffs interpret the [marketing requirement] to be an empty gesture is yet another indication that their submission is erroneous." *Fund for Animals v. Kempthorne*, 472 F.3d 872, 877–78 (D.C. Cir. 2006) (Kavanaugh, J.).

D. CMS properly explained its reasoning for its approach to marketing.

Plaintiffs do not dispute that CMS's reliance on multiple sources of data thwarts any claim that the bona fide marketing standard is arbitrary and capricious based on alleged delay in PDE data. *See* Pls.' Opp. at 43. Plaintiffs instead pivot to a new

argument: that CMS's reliance on multiple sources of data fails to provide "fair warning" of the relevant conduct. *Id.* (citing *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156 (2012)). But a plaintiff cannot raise new claims for the first time in summary-judgment briefing. *See Waugaman*, 841 F. App'x at 433. Plaintiffs have not pled an arbitrary-and-capricious claim regarding alleged failure to provide fair warning, and thus cannot raise such a claim here. *See id.*

In any event, the Revised Guidance provides more-than-sufficient warning about the conduct at issue. The mere fact that CMS leaves open the possibility "to also use other available data and informational sources" to determine whether a generic drug is subject to bona fide marketing does not leave Plaintiffs with any doubt as to *the purpose* for which that data is used. *See* Revised Guidance at 170. Indeed, CMS's reservation of such authority *benefits* Plaintiffs, as it allows CMS to gather a greater variety of evidence regarding marketing.

Finally, Plaintiffs' complaint that the bona fide marketing standard is "illogical and fundamentally unfair"—that is, because it requires more than *de minimis* or sham marketing before de-selection of a drug from the Negotiation Program—rings hollow. Pls.' Opp. at 44. Indeed, Plaintiffs make no response to the Revised Guidance's lengthy discussion of sham agreements that result in generic-drug manufacturers offering only *de minimis* competition. *See* Defs.' MSJ at 43 (citing Revised Guidance at 74). Nor, again, do Plaintiffs disclaim their intent to engage in such practices.

IV. Plaintiffs' due process claim fails because participation in the Negotiation Program is voluntary.

Disposing of Plaintiffs' APA claims leaves only their due process claim. That argument was correctly rejected in *Chamber*, which heeded the essential first step in any procedural-due-process analysis: asking whether there has been a deprivation of a protected property interest. *See Am. Mfrs. Mut. Ins. Co. v. Sullivan*, 526 U.S. 40, 59 (1999). Yet the IRA does not "legally compel[]" participation and therefore cannot effect a deprivation of any protected property interest. *Garelick v. Sullivan*, 987 F.2d 913, 916 (2d Cir. 1993).

Notably, Plaintiffs do not dispute that there are several ways for them to "opt out" of the Negotiation Program. *Chamber*, 2023 WL 6378423, at *11; *see* Pls.' Opp. at 48–49. Both the IRA's text and CMS's implementing guidance confirm that "manufacturers who do not wish to participate in the Program have the ability" to withdraw. *Chamber*, 2023 WL 6378423, at *11; *see also* Revised Guidance at 34. That is fatal to Plaintiffs' due process challenge. Because there is "no constitutional right (or requirement) to engage in business with the government, the consequences of that participation cannot be considered a constitutional violation." *Chamber*, 2023 WL 6378423, at *11.

Plaintiffs attempt to muddy the waters by arguing that *Chamber* is irrelevant because it "turned on" *Michigan Bell Telephone Co. v. Engler*, 257 F.3d 587 (6th Cir. 2001). Pls.' Opp. at 45. To the contrary, *Chamber* expressly turned on the fact that the IRA's Negotiation Program and Medicare are "voluntary" programs such that they cannot effect a constitutional deprivation. *See Chamber*, 2023 WL 6378423, at *10–11. Like Plaintiffs here, the *Chamber* plaintiffs argued that the IRA "strongarm[ed]"

manufacturers into participation in the Negotiation Program. *See id.* at *10. That the plaintiffs attempted to fit that theory into the "confiscatory" due process framework of *Michigan Bell* is irrelevant. *See id.* at *11. Ultimately, the plaintiffs in *Chamber* could not bring a due process challenge because they "are not legally compelled to participate in the Program—or in Medicare generally." *Id.* So too here.

Likewise, it is irrelevant that some of Defendants' cited cases analyzing the voluntariness of participation in Medicare did so in the context of takings claims. *See* Pls.' Opp. at 47. The Takings Clause of the Fifth Amendment, like the Due Process Clause of the Fifth Amendment, applies only where there is legal *compulsion* to surrender property. *See Garelick*, 987 F.2d at 916; *Franklin Mem'l Hosp. v. Harvey*, 575 F.3d 121, 129 (1st Cir. 2009). Whether a program is voluntary is thus dispositive under both the Takings Clause and the Due Process Clause. *See, e.g.*, *Kaiser Found. Health Plan, Inc. v. Burwell*, 147 F. Supp. 3d 897, 911–12 (N.D. Cal. 2015); *Idaho Health Care Ass'n v. Sullivan*, 716 F. Supp. 464, 472 (D. Idaho 1989).

Moreover, economic or other practical "hardship is not equivalent to legal compulsion for purposes of" a Fifth Amendment analysis. *Garelick*, 987 F.2d at 917; *see also St. Francis Hosp. Ctr. v. Heckler*, 714 F.2d 872, 875 (7th Cir. 1983) (the "fact that practicalities may in some cases dictate participation does not make participation involuntary"). Even where "business realities" create "strong financial inducement to participate"—such as, for example, when Medicaid provides the vast majority of a nursing home's revenue—courts have emphasized that the decision to participate in the program "is nonetheless voluntary." *Minn. Ass'n of Health Care Facilities, Inc. v. Minn. Dep't of Pub. Welfare*, 742 F.2d 442, 446 (8th Cir. 1984); *Whitney v. Heckler*, 780 F.2d 963,

972 n.12 (11th Cir. 1986) ("[T]he fact that Medicare patients comprise a substantial percentage of [plaintiff's] practices does not render their participation 'involuntary.'"). So the amount of Plaintiffs' "gross U.S. revenue" obtained through Medicare is irrelevant to the voluntariness analysis. Pls.' Opp. at 49. As the court correctly recognized in *Chamber*, "participation in Medicare, no matter how vital it may be to a business model, is a completely voluntary choice." 2023 WL 6378423, at *11 (discussing cases); *see also Baker Cnty. Med. Servs., Inc. v. U.S. Att'y Gen.*, 763 F.3d 1274, 1280 (11th Cir. 2014).

Notably, Plaintiffs fail to identify a single case supporting the premise that participation in Medicare is involuntary based on the program's lucrative nature. *See generally* Pls.' Opp. at 48–50. For good reason. Congress enacted Medicare, and imposed conditions on participation, pursuant to its Spending Clause powers. "Unlike ordinary legislation, which imposes congressional policy on regulated parties involuntarily, Spending Clause legislation operates based on consent: in return for federal funds, the [recipients] agree to comply with federally imposed conditions." *Cummings v. Premier Rehab Keller, PLLC*, 596 U.S. 212, 219 (2022) (internal quotes and citation omitted). A party cannot be coerced by such an offer because there is no "right (or requirement)" to conduct business with the government in the first instance. *Chamber*, 2023 WL 6378423, at *11; *see, e.g.*, *Shah v. Azar*, 920 F.3d 987, 998 (5th Cir. 2019) ("[P]articipation in the federal Medicare reimbursement program is not a property interest."). "[N]o one has a 'right' to sell to the government that which the government does not wish to buy." *Coyne-Delany Co. v. Cap. Dev. Bd.*, 616 F.2d 341, 342 (7th Cir.

1980); *see also Perkins v. Lukens Steel Co.*, 310 U.S. 113, 127 (1940) (government has authority to "determine those with whom it will deal").

CONCLUSION

For these reasons, the Court should dismiss Counts I and II of Plaintiffs' complaint for lack of subject-matter jurisdiction and enter judgment for Defendants on Count III.

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Respectfully submitted,

BRIAN M. BOYNTON
Principal Deputy Assistant Attorney General

MICHELLE R. BENNETT
Assistant Branch Director

/s/ Cassandra M. Snyder
STEPHEN M. PEZZI
Senior Trial Counsel
CHRISTINE L. COOGLE
CASSANDRA M. SNYDER
ALEXANDER V. SVERDLOV
Trial Attorneys
United States Department of Justice
Civil Division, Federal Programs Branch
1100 L Street, NW
Washington, DC 20005
Tel: (202) 451-7729
Email: cassandra.m.snyder@usdoj.gov

Counsel for Defendants

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/s/ Cassandra M. Snyder
Cassandra M. Snyder
Trial Attorney