PUBLISHED

UNITED STATES COURT OF APPEALS
FOR THE FOURTH CIRCUIT

No. 23-1457

VANDA PHARMACEUTICALS, INC.

Plaintiff - Appellant

v.

CENTERS FOR MEDICARE & MEDICAID SERVICES; CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of Centers for Medicare & Medicaid Services

Defendants - Appellees.

Appeal from the United States District Court for the District of Maryland at Baltimore. Matthew James Maddox, Magistrate Judge. (1:22−cv−00977−MJM)

Argued: January 24, 2024 Decided: April 10, 2024

Before DIAZ, Chief Judge, WILKINSON, Circuit Judge, and MOTZ, Senior Circuit Judge.

Affirmed by published opinion. Judge Wilkinson wrote the opinion, in which Chief Judge Diaz and Senior Circuit Judge Motz joined.

ARGUED: Paul Whitfield Hughes, III, MCDERMOTT, WILL & EMERY, LLP, Washington, D.C., for Appellant. David L. Peters, UNITED STATES DEPARTMENT OF JUSTICE, Washington, D.C., for Appellees. **ON BRIEF:** Andrew A. Lyons-Berg, Alex C. Boota, MCDERMOTT WILL & EMERY LLP, Washington, D.C., for Appellant. Brian M. Boynton, Principal Deputy Assistant Attorney General, Alisa B. Klein, Civil Division, UNITED STATES DEPARTMENT OF JUSTICE, Washington, D.C.; Samuel

R. Bagenstos, General Counsel, Janice L. Hoffman, Associate General Counsel, Susan Maxson Lyons, Deputy Associate General Counsel for Litigation, Kara Wilcox Mundy, UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES, Washington, D.C.; Erek Barron, United States Attorney, OFFICE OF THE UNITED STATES ATTORNEY, Baltimore, Maryland, for Appellees.

WILKINSON, Circuit Judge:

Under the Medicaid Drug Rebate Program, a drug manufacturer that increases its prices faster than inflation rises must reimburse Medicaid for the difference. These reimbursements are paid via rebates. Each drug's rebate amount is usually determined based on its own original price and inflation clock. But not always. Congress has instructed in the Medicaid statute that some "line extension" drugs can be on the hook not only for their own price increases, but also for the price increases of the drugs they evolved from.

In 2020, the Centers for Medicare and Medicaid Services (CMS) promulgated a regulation that set forth criteria for what constitutes a line-extension drug. Vanda Pharmaceuticals challenged that regulation in federal district court, arguing that it expanded the definition of a line extension beyond what the Medicaid statute permitted. The district court disagreed and granted summary judgment to CMS. Because the agency's regulation lies within the bounds of the Medicaid statute, we affirm.

I.

A.

The Medicaid Drug Rebate Program was not built in a day. It was created in 1990, but Congress has regularly revisited the rebate regime in the decades since its enactment. The line-extension provision at issue here was added in one such revision. It is best explained in the context of what came before, and so we begin with a discussion of the program as originally enacted.

Congress created the Medicaid Drug Rebate Program as part of an effort to reduce Medicaid spending. *See* Omnibus Budget Reconciliation Act of 1990, Pub. L. No. 101-508,

tit. IV, subtitle B, pt. 1, 104 Stat. 1388, 1388-141. Congress was concerned that the government was being swindled on drug prices. Medicaid, "the means-tested entitlement program that purchases basic health care for the poor," had been paying significantly more for drugs than other large purchasers. *See* H.R. Rep. No. 101-881, at 96 (1990). To make matters worse, drug prices had been rising rapidly. Between 1981 and 1988 drug price increases had "more than tripled the rate of inflation." *See* Majority Staff of S. Special Comm. on Aging, 101st Cong., *Prescription Drug Prices: Are We Getting Our Money's Worth?* 8 (Comm. Print 1989). Congress devised the new rebate program in response to both these problems.

Under the program, drug manufacturers must pay rebates to Medicaid that offset part of the cost of the manufacturers' drugs, thus lowering the ultimate price Medicaid pays. The rebate amounts are calculated by CMS, but the Medicaid statute meticulously lays out the formula that CMS must use. It has two components. The first (which is not at issue here) is the "basic rebate," which ensures that Medicaid pays the lowest price for any given drug. *See* 42 U.S.C. § 1396r-8(c)(1).

This case concerns the "additional rebate," which forces drug manufacturers to reimburse Medicaid for price increases greater than the rate of inflation. § 1396r-8(c)(2). It is calculated by taking the difference between the current average price of the drug and the price of the drug when it was first marketed, adjusted for inflation. *See* § 1396r-8(c)(2)(A). In other words, once a drug manufacturer sets an initial price for a drug, Medicaid will not pay more than that price (plus inflation). Medicaid thus locks in that original price.

But the original additional rebate formula had a loophole. The statute calls for a separate rebate calculation for "each dosage form and strength" of a covered drug. *Id*. A manufacturer could thus raise the price of a drug without paying the additional rebate by releasing a new strength (or form) of the drug at a higher price. The additional rebate for the new strength would be based on the new strength's higher release price rather than the original one. The manufacturer could then discontinue the original strength, forcing purchasers to switch. As a result, the manufacturer could avoid reimbursing Medicaid for the jump in price. *See* H.R. Rep. No. 111-299, pt. 1, at 635 (2009); S. Rep. No. 111-89, at 92 (2009).

Congress added the line-extension provision in 2010 in part to close this loophole. It provides that so-called "line extension" drugs are on the hook not only for their own price increases, but also for any price increases to the original drug on which they were based. Here is how the provision works: For a line-extension drug, the additional rebate is the greater of two amounts. Amount One depends on the price increases of the *line-extension drug* and is calculated the same way as above—that is, by taking the difference between the current average price of the line-extension drug and the price of that drug when first marketed, adjusted for inflation. § 1396r-8(c)(2)(C)(ii). So far, so good. A line-extension drug is treated just like any other drug.

Amount Two, however, depends on whether the price of the *original drug* has increased. It is calculated by multiplying the highest additional rebate percentage owed on any strength of the original drug by the price of the line-extension drug. *See* § 1396r-8(c)(2)(C)(iii). In other words, Medicaid will treat the line-extension drug as if its

own price had increased proportionally with the original drug's. For example, if one of the strengths of the original drug (taking inflation into account) had doubled in price since its release, the line-extension drug would also be treated as if it had doubled in price and would thus be subject to at least a 50% rebate, regardless of whether the price of the line-extension drug had changed at all. Importantly, because the statute instructs that the additional rebate for a line extension is the greater of Amount One and Amount Two, line-extension status can only lead to higher rebates.

B.

But what *is* a line extension? Answering that question involves consulting two sources: the Medicaid statute and the corresponding CMS regulation challenged in this case.

1.

First, the guidance given by Congress: According to the Medicaid statute,

> [T]he term "line extension" means, with respect to a drug, a new formulation of the drug, such as an extended release formulation, but does not include an abuse-deterrent formulation of the drug (as determined by the Secretary), regardless of whether such abuse-deterrent formulation is an extended release formulation.

§ 1396r-8(c)(2)(C)(iii).

To break that down, the statute instructs that a "line extension" is a "new formulation" of an existing drug. There is also a carveout: abuse-deterrent formulations do not count. (The carveout was added in 2016 as part of Congress's response to the opioid crisis. *See* Comprehensive Addiction and Recovery Act of 2016, Pub. L. No. 114-198, § 705(a), 130 Stat. 695, 753.) As is clear from this statutory language, however, the

legislative definition of line extension is incomplete: Congress inserted the language "such as" before providing the example of "an extended release formulation," indicating a gap left to be filled. As is common in administrative regulation, the agency charged with carrying out the program (here, CMS) was left to fill in the blanks.

The Medicaid statute provides one more wrinkle important to the case at hand. The line-extension provision (and the higher rebates it brings) does not apply to *all* line-extension drugs. It applies only to "a line extension of a single source drug or an innovator multiple source drug that is an oral solid dosage form." § 1396r-8(c)(2)(C)(i). In simpler terms: the provision applies only to line extensions of two specific types of drugs (defined later in the statute), and only to a "line extension of [either of those types of drugs] that is *an oral solid dosage form*." *Id.* (emphasis added). This oral-solid-dosage-form requirement presented a puzzle: which drug(s) must be in oral solid dosage form? The original drug? The line-extension drug? Both? Here, too, it fell to the implementing agency to resolve the ambiguity.

2.

CMS took up those twin calls in June 2020. The agency had received "requests to provide more specific guidance on how to identify a line extension drug." 85 Fed. Reg. 37,286, 37,294 (June 19, 2020). The agency also had reasons to think that a more explicit definition of line extension was necessary. "After several years of experience with manufacturers self-reporting their line extensions," it had "noted inconsistency among manufacturers." *Id.* The agency suspected that line extensions were being underreported because "manufacturers may have a financial incentive to be underinclusive in their

identification." *Id.* It therefore proposed a regulation that would "interpret the term 'line extension' broadly." *Id.* at 37,295. After notice and comment, the agency finalized its proposal (with modest changes) in December 2020.

The final regulation started with a definition for line extension that closely tracks the statute:

> *Line extension* means, for a drug, a new formulation of the drug, but does not include an abuse-deterrent formulation of the drug (as determined by the Secretary).

85 Fed. Reg. 87,000, 87,101 (Dec. 31, 2020) (codified at 42 C.F.R. § 447.502). It also defined the term "new formulation" and expanded on the example from the statute:

> *New formulation* means, for a drug, a change to the drug, including, but not limited to: an extended release formulation or other change in release mechanism, a change in dosage form, strength, route of administration, or ingredients.

Id. at 87,101–02 (codified at 42 C.F.R. § 447.502).

The agency's regulation also clarified its understanding of the oral-solid-dosage-form requirement: "only the initial brand name listed drug must be an oral solid dosage form." *Id.* at 87,034. In other words, only the *original* drug needs to be in an oral solid dosage (read: pill) form for the provision to apply. The *line-extension* drug can be in a different form—liquid, say, or injectable—and still qualify for the new rebate formula.

On this point, however, the agency has wavered. In 2012, it had proposed that both the line-extension drug *and* the original drug must be in oral solid dosage form. *See* 77 Fed. Reg. 5318, 5338 (Feb. 2, 2012). But it declined to finalize that proposal. *See* 81 Fed. Reg. 5170, 5265 (Feb. 1, 2016). In its 2020 rulemaking, CMS changed course, proposing in June

and finalizing in December after notice and comment that the requirement applied to only the original drug.

C.

Appellant Vanda was not happy with the agency's new moves. Vanda develops and manufactures innovative drugs that treat rare disorders. Its two flagship drugs are Hetlioz and Fanapt, each of which has a sister drug that Vanda worries will be swept up in the agency's new line-extension definition.

Hetlioz is a drug approved to treat (among other conditions) severe sleep disturbances caused by the developmental disorder Smith-Magenis syndrome. This disorder affects both adults and children, but Hetlioz is approved only for adults because it comes in oral solid dosage form (a pill capsule), and the dosage cannot be calibrated to children's weights. So Vanda created a liquid version called Hetlioz LQ for use in treating sleep disturbances in children with Smith-Magenis syndrome. Hetlioz LQ was approved by the Food and Drug Administration (FDA) in 2020 and is available today for patients 3 to 15 years of age.

Vanda also manufactures Fanapt, an antipsychotic used to treat schizophrenia. Fanapt is currently offered in pill form and must be taken twice a day. Like many antipsychotics, it is safest and most effective if taken at regular intervals without missing a dose. But people with schizophrenia often struggle to adhere to such treatment regimens. To solve this problem, Vanda has been working to create a long-acting injectable version of Fanapt called Fanapt LAI. Fanapt LAI is still in development, but Vanda hopes to offer it in a format that would require patients to receive only a few injections each year.

According to Vanda, this change could "revolutionize schizophrenia treatment." Appellant's Opening Br. 16.

Vanda alleges that, under the agency's pre-regulation approach, neither Hetlioz LQ nor Fanapt LAI would have been considered line extensions. Under the new regulation, however, both will be.

Vanda has a strong interest in avoiding line-extension status for its drugs. Many patients who use Vanda's drugs are enrolled in Medicaid. Fanapt users are especially likely to be Medicaid recipients, as 70% of people with schizophrenia are covered under the program. *See* Kimberly H. Geissler et al., *Differences in Insurance Coverage for Individuals with Schizophrenia After Implementation of the Patient Protection and Affordable Care Act*, 80(3) JAMA Psychiatry 278, 278–79 (2023); *see also* Appellant's Opening Br. 17. Medicaid sales are thus an important source of revenue for Vanda, and Medicaid rebates cut into profits. Line-extension status can trigger even higher rebates, which Vanda would prefer to avoid. To that end, Vanda seeks to cabin the definition of line extension so as to exclude drugs like Hetlioz LQ and Fanapt LAI.

D.

Vanda sued in U.S. District Court to challenge the agency's 2020 regulation. It argued that the regulation's definitions of "line extension" and "new formulation" were contrary to the text of the Medicaid statute. It also challenged the agency's new interpretation of the oral-solid-dosage-form requirement. Finally, Vanda alleged that the agency had violated the Administrative Procedure Act (APA) because the agency failed to

adequately address important industry concerns aired during the notice-and-comment period.

On cross-motions for summary judgment, the district court rejected Vanda's claims. It held that the regulation was consistent with the text of the Medicaid statute, and that CMS had satisfied its obligations under the APA. *See Vanda Pharms., Inc. v. Ctrs. for Medicare & Medicaid Servs.*, 2023 WL 2743364, at *16, 18, 23–24 (D. Md. Mar. 31, 2023). Vanda timely appealed.

II.

Under the APA, we set aside an agency's regulation only if it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). We review the district court's evaluation *de novo*, independently assessing whether the agency action was unlawful. *See Ren v. U.S. Citizenship & Immigr. Servs.*, 60 F.4th 89, 93 (4th Cir. 2023).

III.

Vanda first argues that the 2020 regulation is "not in accordance with law," § 706(2)(A), because it broadened the sweep of the line-extension provision beyond what the Medicaid statute permits. We are thus called upon to evaluate whether the 2020 regulation contravenes the Medicaid statute's text. That task, however, presents a conundrum. Courts have traditionally reviewed an agency's statutory interpretations in accordance with the two-step framework of *Chevron U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). *See, e.g.*, *Cela v. Garland*, 75 F.4th 355, 360–61 (4th Cir. 2023). Under that framework, we would first "consider[] 'whether Congress

has directly spoken to the precise question at issue.'" *Id.* at 361 (quoting *Chevron*, 467 U.S. at 842). If so, our inquiry would stop there. If the statute was ambiguous, however, we would defer to the agency's interpretation so long as it was reasonable. *Id.*

But CMS did not invoke *Chevron* in its briefing or at oral argument. Recent Supreme Court precedent has made clear that if the "government is not invoking *Chevron*" a court can "decline to consider whether any deference might be due." *HollyFrontier Cheyenne Ref., LLC v. Renewable Fuels Ass'n*, 141 S. Ct. 2172, 2180 (2021); *see also Guedes v. Bureau of Alcohol, Tobacco, Firearms, & Explosives*, 140 S. Ct. 789, 789–90 (2020) (Gorsuch, J., statement respecting the denial of certiorari) (explaining that the Supreme Court "has often declined to apply *Chevron* deference when the government fails to invoke it" and collecting cases).

We, of course, follow the Supreme Court's lead here. Thus, if we encounter statutory ambiguity, rather than deferring to the agency's interpretation, we will "approach [that] interpretive problem[] methodically, using traditional tools of statutory interpretation." *Facebook, Inc. v. Duguid*, 592 U.S. 395, 404 n.5 (2021). In doing so, however, we will "pay particular attention to [the] agency's views in light of the agency's expertise in [the] given area" and "its knowledge gained through practical experience." *County of Maui v. Haw. Wildlife Fund*, 140 S. Ct. 1462, 1474 (2020). But we will adopt those views as our own only if they have the "power to persuade." *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944).

With those principles in mind, we turn to Vanda's claims. It challenges two parts of the agency's 2020 regulation: the definitions of line extension and new formulation, and

the agency's understanding of the oral-solid-dosage-form requirement. We take each in turn.

A.

We begin with Vanda's claim that the 2020 regulation is contrary to law in that it gives impermissible definitions to the terms "line extension" and "new formulation." Generally, Vanda argues that the agency's broad definitions contravene the purportedly narrow focus of the line-extension provision in the Medicaid statute. Vanda then offers up two specific limitations that it reads into the statutory regime. We take up the general point first.

1.

We disagree with Vanda's contention that the agency's definitions stray outside the general statutory ambit. Start with the definition of line extension. We are struck at the outset by the similarities in the statutory and regulatory definitions of this term. In contrast to Vanda's claims, the substance of the regulatory definition hews quite closely to the statute. Both define "line extension" as a "new formulation" and then carve out an exception for "abuse-deterrent formulation[s]." *Compare* § 1396r-8(c)(2)(C)(iii), *with* 42 C.F.R. § 447.502.

The similarities are so striking as to make this part of the regulation unimpeachable. Each departure of the regulatory text is patently superficial, with no discernable effect on the term's reach. The agency's definition of line extension is clearly within the bounds of the statute and we see no reason it should be set aside.

We turn next to the definition of new formulation. Vanda claims that here the regulation strays further afield, but it is plainly not so far as to call "foul ball." Recall that the statute explains the term by reference to a single example: "an extended release formulation." § 1396r-8(c)(2)(C)(iii). That example, however, is introduced with the inclusive phrase "such as," making clear that Congress intended the term to sweep more broadly than the illustrative example it chose.

The regulation thus starts with a broader definition: a "new formulation" is "a change to the drug." 42 C.F.R. § 447.502. It then provides an expanded list of changes that can count. The list starts with the statutory example of "an extended release formulation." But it adds "other change[s] in release mechanism" and changes in "dosage form, strength, route of administration, or ingredients" as well. *Id.* And like the statute, the regulation makes clear (here with the phrase "including, but not limited to") that those examples are meant to be illustrative, not exhaustive. *Id.*

This strikes us as a perfectly sensible way to implement the regime set by the Medicaid statute. Start with the term Congress chose: "a new formulation." Something is "new" if it is "different from [what] previously exist[ed]." *New*, Oxford English Dictionary (2d ed. 1989). And a "formulation" is "a material or mixture prepared according to a particular formula." *Formulation*, Oxford English Dictionary (2d ed. 1989) (emphasis added). Putting it all together, a new formulation is created whenever a drug is prepared according to a formula different from the formula or formulas previously in use. A *different* formula creates a *new* formulation.

The agency's choice to define a "new formulation" as a "change" aligns quite closely with the words selected by Congress. With respect to drugs, change is achieved precisely by using a different formula. Drug manufacturers often create several variations of a drug. A drug may come as a pill, a rapid release gel, a chewable, a dissolve pack, or in a liquid suspension measured out with a little plastic cup. As each successive format is developed, the drug must be *changed* by using a *different formula* to achieve each final product. It makes perfect sense, then, to say that each new iteration achieved by such a change might permissibly be termed a "new formulation."

Vanda, though, takes aim at the breadth of the definition. It says the agency's definition sweeps in too much, pointing for support to the Congressional Budget Office report in which a line-extension provision was first suggested. *See* CBO, *Budget Options, Volume I: Health Care* 143 (Dec. 2008) (the "CBO Report"). The report stated that drug manufacturers could "avoid incurring an additional rebate obligation by making a slight alteration to an existing product." *Id.* It recommended that Congress close this "loophole" by treating "a certain type of new formulation—specifically, extended-release versions" more like "the original product." *Id.* This, Vanda says, was the problem Congress intended to solve with the line-extension provision as well: drug manufacturers avoiding the additional rebate by making merely incremental changes to their original drugs to reset the inflation clock. And so, according to Vanda, Congress must have intended the term "new formulation" only to encompass such slight alterations. Vanda insists that larger changes in formula create altogether new drugs—not simply line extensions to original drugs—and that therefore such changes should not fall into the provision's reach.

We do not think that this is a fair reading of the statute or a fair condemnation of the agency's regulation. As an initial matter, "legislative history is not the law." *Azar v. Allina Health Servs.*, 139 S. Ct. 1804, 1814 (2019). Courts must "apply faithfully the law Congress has written" and "cannot replace the actual text with speculation as to Congress' intent." *Luna Perez v. Sturgis Pub. Sch.*, 598 U.S. 142, 150 (2023). And the law that Congress passed differs in important respects from the Budget Office proposal cited by Vanda. That proposal would have gone after extended-release formulations only, whereas the statute makes clear that extended-release formulations are but one example of what will be swept in. And the proposal targets "a *certain type* of new formulation." CBO Report, at 143. In contrast, the statute speaks in terms of new formulations writ large.

The 2016 amendment that carved out abuse-deterrent formulations confirms that the statutory definition is broader than Vanda would have it be. Abuse-deterrent formulations are not slight, meaningless alterations. They require new innovations and costly research and development. They also provide important therapeutic benefits and help prevent the harmful consequences attendant to prescription drug misuse. The fact that they had to be carved out from the provision shows that the statutory definition encompasses more than just the meaningless changes Vanda advocates.

And Vanda's argument overlooks the fact that Congress chose to define line extension as a "new formulation." Vanda says that an alteration that is more than slight creates, not a new formulation, but an entirely new drug. But the term "new formulation" does not by its plain meaning limit line extensions in the way Vanda might hope. We use the term "new" to describe differences both big and small, and both types of changes can

create an updated version of an original without creating an entirely novel item. Take as an example the new editions of well-loved books. Sometimes the differences are atmospheric or slight. Oxford World's Classics' new edition of Willa Cather's *My Ántonia* added a new introduction and notes that provide historical context, but Cather's evocative descriptions of pioneer life on the plains of Nebraska remain intact. *See* Willa Cather, *My Ántonia* (Oxford World's Classics ed. 2009). In other words, despite peripheral changes, the substance of the book remains the same. But sometimes the differences in new versions of something can be quite large indeed. New editions of classic legal treatises can differ dramatically from the old, especially when there have been major intervening changes in doctrine. But that does not mean that the fourth edition of *Williston on Contracts* cannot be said to be a "new edition" with respect to the third. Even significant changes, therefore, can still flow from the original so long as there is a throughline between them. Congress's choice of the definition "new formulation" simply fails to support Vanda's contention that anything more than a "slight alteration" should count as a new drug entirely.

Moreover, the structure of the statutory line-extension provision confirms that a broad definition of new formulation is appropriate. The statutory provision speaks in terms of inclusion, not exclusion. It makes clear that a line extension is "a new formulation of the drug, *such as* an extended release formulation." § 1396r-8(c)(2)(C)(iii) (emphasis added). Terms of inclusion like "such as" are congressional invitations for agencies to apply their expertise to fill out the list with further examples. "Congress knows to speak in plain terms when it wishes to circumscribe, and in capacious terms when it wishes to enlarge, agency

discretion." *City of Arlington v. FCC*, 569 U.S. 290, 296 (2013). Here, Congress chose the broader route and reinforced it with a structure evincing inclusive intent.

The agency heeded the congressional invitation. When proposing the regulation at issue here, the agency acknowledged that it had chosen a "much broader definition of new formulation" than in previous (never-finalized) proposals. *See* 85 Fed. Reg. at 37,295. It also made clear that its broadened definition was designed to expand the universe of drugs that qualified as line extensions. *Id.* The agency "believe[d] that the statute g[ave] [it] discretion and authority to interpret the term 'line extension' broadly" and to "include a broad range of drugs" therein. *Id.* In response to "requests to provide more specific guidance," *id.* at 37,294, the agency informed manufacturers that—in addition to extended-release formulations—"other change[s] in release mechanism" and changes in "dosage form, strength, route of administration, or ingredients" would count as line extensions too. 42 C.F.R. § 447.502.

We find the agency's additional examples here "reasonable" and "consistent with the statutory framework." *Fed. Exp. Corp. v. Holowecki*, 552 U.S. 389, 402 (2008). In fact, the agency's added examples strike us as fairly similar to extended-release formulations. And we can think of no "clearer alternatives" that are "within our authority or expertise to adopt." *Id.* Moreover, Vanda has not identified any individual element of the list that poses a particular problem. In short, then, we do not find merit in Vanda's general challenge to the breadth of the agency's "new formulation" definition.

That is not to say, however, that the agency is subject to no limitations at all. Line-extension status is relational. A drug product cannot be a line extension in the abstract; it

is a line extension of a particular original drug. *See* § 1396r-8(c)(2)(C)(iii) ("[T]he term "line extension" means, *with respect to a drug*, a new formulation *of the drug*." (emphasis added)). The two must bear some relationship to each other. And not all relationships will suffice. Tylenol (active ingredient: acetaminophen) is not a line extension of Advil (active ingredient: ibuprofen), even though both are useful in treating aches and pains.

Luckily, we need not confront the problem of when changes to a drug are significant enough to take it from a new formulation to a distinct drug entirely. The agency's chosen examples of changes—different release mechanisms, routes of administration, dosages, ingredients, and strengths—are limited enough (and similar enough to extended-release formulations) to fit well within the statutory bounds.

2.

In addition to taking aim at the breadth of the provision generally, Vanda proposes two specific textual limitations on the term "line extension." We find neither one persuasive.

First, Vanda looks to the definitions of the words "line" and "extension" to argue that a line extension must serve the same "purpose" as an existing drug. For support, it states that the definition of line is "material serving a particular purpose." Appellant's Opening Br. 36. But the full text of the cited definition is: "*a length of cord, rope, wire, or other* material serving a particular purpose." *Line*, New Oxford American Dictionary (3d ed. 2010) (emphasis added). And the examples given relate to telephone lines or lines of cord used for hanging out the wash to dry. *Id.* We are skeptical that this is the definition that Congress had in mind. A more on-point definition is "merchandise or services *of the*

same general class for sale or regularly available." *Line*, Merriam-Webster's Collegiate Dictionary (10th ed. 1999) (emphasis added). Tellingly, this definition is broader than what Vanda proposes.

Second, Vanda points out that the agency's broad definition of line extension would sweep in drugs for which the FDA requires a new drug application. It urges us to hold that those drugs are not new formulations, but new drugs themselves ineligible for line-extension status. But extended-release formulations (which, recall, are explicitly listed in the statute as new formulations) sometimes require just such new drug applications. That alone shows that a new drug application is not the silver bullet Vanda imagines.

In making its new-drug-application point, Vanda fails to consider the phrase "new formulation of the drug" as a whole. Instead, Vanda counsels that Congress's insertion of the words "the drug" provides an oblique cross-reference to the oral-solid-dosage-form requirement. Only by looking there, according to Vanda, can we understand what "the drug" must mean. In *that* requirement, Vanda continues, the statute mentions two types of drugs: "single source drug" and "innovator multiple source drug." From there, Vanda instructs that we should look at the definitions portion of the Medicaid Drug Rebate Program to find out what qualifies a drug as either of those types. And (in a final step) Vanda points out that both these types of covered drugs must fall "under a new drug application approved by the Food and Drug Administration." §§ 1396r-8(k)(7)(A)(ii), (iv).

According to Vanda, this lengthy chain of cross-references establishes some sort of statutory instruction that no drug marketed under a new drug application can ever be a line

extension because such a drug is always an original drug instead. Line extensions, on Vanda's reading, can therefore only be drugs for which the FDA requires a *supplemental* new drug application.

This argument is wholly unpersuasive. The FDA has a different focus from the Medicaid Drug Rebate Program. The FDA is concerned chiefly with the safety and efficacy of drugs, not with their cost. And the cross-references to the FDA approval process in the definitions of the Medicaid Drug Rebate Program are meant chiefly to limit Medicaid drug coverage to drugs that the FDA considers safe and efficacious—not to create a hidden constraint on line extensions.

If Congress had meant to limit line extensions to drugs approved via supplemental new drug applications, we think it would have done so explicitly within the definition of the term "line extension." *See Jama v. Immigr. & Customs Enf't*, 543 U.S. 335, 341 (2005) ("We do not lightly assume that Congress has omitted from its adopted text requirements that it nonetheless intends to apply, and our reluctance is even greater when Congress has shown elsewhere in the same statute that it knows how to make such a requirement manifest."). Other provisions of the Medicaid Drug Rebate Program do explicitly depend on FDA determinations: Special reimbursement limits apply when the FDA has rated several drugs as "therapeutically and pharmaceutically equivalent." § 1396r-8(e)(4). And drugs "approved by the [FDA] exclusively for pediatric indications" are eligible for a lower minimum rebate. § 1396r-8(c)(1)(B)(iii)(II)(bb). No such FDA references are made in the line-extension definition at issue here. That definition is at the core of the matter. In contrast, Vanda's argument invokes provisions that are wandering on the periphery.

* * *

Having addressed Vanda's arguments to the contrary (both general and specific), we find that the agency's definitions of line extension and new formulation are appropriately within the Medicaid statute's ambit. We thus affirm the district court as to this aspect of the case.

B.

We turn now to Vanda's challenge to the portion of the agency regulation regarding the oral-solid-dosage-form requirement. Recall that the line-extension provision applies only to "a drug that is a line extension of a single source drug or an innovator multiple source drug that is an oral solid dosage form." § 1396r-8(c)(2)(C)(i). The agency and Vanda disagree about whether the oral-solid-dosage-form requirement applies only to the original drug ("a single source drug or an innovator multiple source drug") or to the line-extension drug as well.

The agency states that the modifier "that is an oral solid dosage form" applies only to the immediately preceding phrase "a single source drug or an innovator multiple source drug." The regulation therefore instructs that "only the initial brand name listed drug must be an oral solid dosage form." 85 Fed. Reg. at 87,034. The line-extension drug, according to the agency, can be in any form at all.

Vanda disagrees. It asserts that the agency's reading is contrary to the statute and proposes that *both* the original drug *and* the line-extension drug must be in oral solid dosage form for the provision to apply.

The agency's interpretation is the more persuasive. The statute makes clear that only one thing need be "an oral solid dosage form" by using the singular verb "is." Verbs in modifying phrases must correspond to their intended antecedent: If the antecedent is singular, the verb must be singular. If the antecedent is plural, the verb must be plural. *See* Rodney Huddleston & Geoffrey K. Pullum, *The Cambridge Grammar of the English Language* § 18.1, p. 500 (2002). Thus a visitor to a local café can order a single cappuccino that *is* made with whole milk, but if she wants two she will need to ask the barista for cappuccinos that *are* made with whole milk. Vanda's reading, on which two drugs must meet the requirement, violates this grammatical rule.

In contrast, the agency's reading conforms with the rule. According to the agency, only one thing—the original drug—must be in oral solid dosage form. And, grammatically, it is of no moment that the original drug can be either "a single source drug or an innovator multiple source drug." When singular nouns are joined by words like "or," they take a singular verb. *See id.* § 18.4(b), p. 508.

The agency's reading also comports with the last antecedent rule, which counsels that a limiting clause "should ordinarily be read as modifying only the noun or phrase that it immediately follows." *See Barnhart v. Thomas*, 540 U.S. 20, 26 (2003). Here, the phrase "that is an oral solid dosage form" immediately follows the phrase "a single source drug or an innovator multiple source drug." That phrase consists of a series of two specific terms with "straightforward, parallel construction." Antonin Scalia & Bryan A. Garner, *Reading Law: The Interpretation of Legal Texts* 147 (2012). And so the modifier at the end of that list should be read to "appl[y] to the entire series." *Id.*; *see also Facebook*, 592 U.S. at 402–

03. The "most natural reading" is thus that the oral-solid-dosage-form requirement applies to the two elements in the parallel series before it: single source and innovator multiple source drugs. *See Facebook*, 592 U.S. at 403. That suggests that the original drug (whether a single source drug or an innovator multiple source one) is the thing that must be in oral solid dosage form.

We think the agency persuasively posits that the last antecedent rule applies here. Vanda protests, however, that the last antecedent rule does not apply to an "'integrated' clause" that "refer[s] to a single thing." *Cyan, Inc. v. Beaver Cnty. Emps. Ret. Fund*, 583 U.S. 416, 440 (2018). The phrase "a line extension of a single source drug or an innovator multiple source drug," Vanda continues, is just such an integrated clause. But even so, this does not support Vanda's suggested reading. When faced with integrated clauses, the Supreme Court has instructed that "the modifier goes back *to the beginning* of the preceding clause." *Id*. (emphasis added). And so, even if we were to read the phrase at issue as an integrated clause, *only* the line extension (and *not* the original drug) would need to be in oral solid dosage form. But Vanda's position is that *both* drugs must be. Even Vanda's proposed exception to the last antecedent rule does not support its preferred result.

Vanda lastly tries to avoid the most obvious grammatical reading by contending that the agency's interpretation would produce an "absurd" result: that pill-to-liquid transformations can lead to line extensions, but liquid-to-pill transformations cannot. It is true that the Supreme Court will sometimes reject "the most grammatical reading" of a statute when it would produce a result that is "positively absurd." *United States v. X-Citement Video, Inc.*, 513 U.S. 64, 69–70 (1994). But only when the absurdity is quite

serious indeed. *See, e.g.*, *id.* (rejecting the most grammatical reading because it would raise "substantial constitutional questions" and impose criminal penalties without any scienter requirement). We see no such absurdity here. A great many drugs start off as pills. And new formulations can work off that initial form as well. It was reasonable for Congress to target this common path of transformation. Further, judicial rulings that Congress produced an "absurdity" must be rare indeed, lest we open the gates for our own policy preferences to trump those chosen by the legislature.

In short, and fundamentally, Vanda's reading cannot be squared with the language of the statute. It has therefore failed to demonstrate that the agency's interpretation of the oral-solid-dosage-form requirement was contrary to law. We thus affirm the district court and uphold the agency's regulation as to the oral-solid-dosage-form requirement as well.

IV.

Having concluded that the regulation is not contrary to law, we turn to Vanda's contention that the agency's rulemaking here was arbitrary and capricious in violation of the APA. Unlike contrary-to-law analysis, arbitrary and capricious review is "very deferential." *Rural Cellular Ass'n v. FCC*, 588 F.3d 1095, 1105 (D.C. Cir. 2009). It is focused not on the substance of the regulation, but on "the reasonableness of the agency's decisionmaking processes." *Id.* We look only to whether the agency has "reasonably considered the relevant issues and reasonably explained the decision" it made. *FCC v. Prometheus Radio Project*, 592 U.S. 414, 423 (2021).

Vanda lodges three specific complaints against the procedure undergirding the agency's 2020 regulation. First, Vanda contends that the agency failed to confront a

"practical inconsistency" that results from the agency's construction of the oral-solid-dosage-form requirement, reiterating its view that it would be "absurd" for the line-extension provision to apply to transformations from pill to liquid but not from liquid to pill. But, given our discussion above, *see supra* III.B, any such inconsistency must be laid at the feet of Congress, not the agency. This, then, cannot be cited as a flaw in the agency's rulemaking procedure.

Second, Vanda accuses the agency of failing to account for reliance interests engendered by its 2012 proposal. But the agency explicitly declined to finalize that proposal and instructed manufacturers instead to "rely on the statutory definition." 81 Fed. Reg. at 5265. The notice-and-comment procedure is designed so that an agency can float a potential rule to the public without committing itself to enacting the proposed rule's content. We are thus loath to impose on agencies an obligation to make allowances for industry players who relied on proposals never implemented. Such an obligation would only serve to dissuade agencies from making exploratory proposals in the first place. The agency here acknowledged that it was changing its position, *see* 85 Fed. Reg. at 87,034, and explained that the new interpretation was based on "10 years' experience" and "supported by the statute," *id.* at 87,036. That was sufficient to satisfy the APA.

Finally, Vanda accuses the agency of failing to consider the "chilling effects on pharmaceutical innovation." Appellant's Opening Br. 23. But in alleging such effects, Vanda overlooks two things. First, line-extension status leads to higher rebates only if a drug manufacturer chooses to raise the price of the original drug at a rate that outpaces inflation. Drug manufacturers are thus in control of the rebate that they pay. Second, a drug

manufacturer can set the initial price for a line-extension drug as high as it needs to recoup the cost of its development, and can increase that price as well so long as those increases do not outpace inflation either. As the agency explained, a line-extension drug incurs a higher rebate "not due to the innovations in the new formulation" but "because the *original* drug increased in price faster than the rate of inflation." 85 Fed. Reg. at 87,041 (emphasis added). The agency also rightly noted that if Congress had intended for factors such as "the extent of the improvements" or "the value of an innovation" to "limit the scope of drugs that are line extensions, it would have provided as much in the statute." *Id.* at 87,038. We think this satisfies the agency's burden under the APA to respond to innovation-focused comments and concerns.

In sum, none of the challenges Vanda raises to the agency's decision-making process suffice to show that the agency acted arbitrarily or capriciously. We therefore hold that the process conformed to the APA's strictures and affirm the district court with respect to Vanda's claim here as well.

V.

It is not surprising that the government advocates a broad definition of line extension, both in the regulation and in this litigation. Line-extension status makes a big difference to the federal purse. It creates the prospect of larger inflation-based rebates, which make up an increasingly large portion of the total amount paid under the Medicaid Drug Rebate Program—more than half since 2012. *See* Off. of Inspector Gen., U.S. Dep't of Health & Hum. Servs., *Medicaid Rebates for Brand-Name Drugs Exceeded Part D Rebates by a Substantial Margin,* OEI-03-13-00650 (Apr. 2015).

Inflation-based rebates account for so much of the total amount rebated not because of choices the agency has made, but because prescription drug prices continue to rise. Recall that when Congress was considering the Medicaid Drug Rebate Program, a Senate report noted that drug prices had been increasing at three times the rate of inflation. This problem has not abated. Between January 2022 and January 2023, drug prices increased an average of 15.2%. *See* U.S. Dep't of Health & Hum. Servs., *Changes in the List Prices of Prescription Drugs, 2017-2023* (Oct. 6, 2023). That is still nearly three times the 6.4% rate of inflation measured for the same period. *See* U.S. Bureau of Lab. Stats., *Consumer Prices for Shelter Up 7.9 Percent from January 2022 to January 2023* (Feb. 16, 2023).

Congress reasonably sought to respond to these soaring costs via innovative solutions, such as the line-extension provision at issue here. In recent years, Congress has doubled down on this mission to control drug prices while preserving the ability of pharmaceutical companies to grow their research and development. Indeed, post-regulation initiatives underscore this continuing focus. The Inflation Reduction Act of 2022 established for *Medicare* a rebate program based on the *Medicaid* Drug Rebate Program at issue in this litigation. *See* Pub. L. No. 117-169, § 11102, 136 Stat. 1818, 1871 (codified at 42 U.S.C. § 1395w-114b). The new Medicare rebate provision, like its Medicaid counterpart, includes a line-extension provision corresponding to the one before us. *See* § 1395w-114b(b)(5)(B)(ii). And it instructs the agency that the Medicare rebate formula should match the one the agency uses in Medicaid. *See* § 1395w-114b(b)(5)(B)(i).

Post-regulation initiatives do not operate as any sort of ironclad proof of original congressional intent to broaden the universe of drug-expenditure regulation. If the agency's

regulation was at odds with the line-extension provision in the statute, post-enactment events in other statutes could not salvage it. *See Food Mktg. Inst. v. Argus Leader Media*, 139 S. Ct. 2356, 2366 (2019). But the fact that Congress is pushing in the same direction as the agency to carefully balance progress and prices strengthens our conviction that the statute it enacted allows for the regulation the agency imposed.

Inflation-based rebates, of course, are not permissible as a matter of policy but only insofar as they conform to law. But given that costs have continued to rise and that Congress has continued to expand its cost-control measures, we think the balance struck by the agency's challenged regulation between cost control and room for pharmaceutical innovation is appropriate. By entrusting the Medicaid Drug Rebate Program to CMS's care, Congress charged the agency with trying to provide some modest set of controls on healthcare costs to the government at a time when great medical advances bring great benefits but also impose great expense. Vanda is entitled to disagree with the balance struck, but we do not think that the statute gives us the authority to upset that balance so long as it operates within the margins Congress drew. If Vanda prefers a different balance between these competing forces, it should direct its arguments to Congress, not to the federal courts.

Our job is simply to ensure that the agency's rule is not contrary to law. In this case, we think that the agency's rule is in accord with law for all the reasons set forth above. The district court's judgment is thus

AFFIRMED.