No.

In the Supreme Court of the United States

VANDA PHARMACEUTICALS INC.,

Petitioner,

v.

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

Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Fourth Circuit

PETITION FOR A WRIT OF CERTIORARI

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QUESTIONS PRESENTED

This case addresses the "line extension" provision of the Medicaid rebate statute. For a decade, CMS construed the statute as written, covering drugs introduced as gamesmanship to avoid a penalty provision. Recently, however, CMS adopted a regulatory definition of "line extension" that, by the agency's own admission, was "much broader" than its earlier views.

In so doing, CMS failed to recognize a key statutory constraint on its authority. Per Congress, the "line extension" provision applies to "a single source drug or an innovator multiple source drug." 42 U.S.C. § 1396r-8(c)(2)(C)(i). Congress established that "the term 'line extension' means, with respect to a drug, a new formulation of the drug." *Id*. § 1396r-8(c)(2)(C). The new formulation, accordingly, must be the *same drug* as the original. Congress tethered this inquiry to "a new drug application approved by" FDA. *Id*. §§ 1396r-8(k)(7)(A)(ii) & (iv). If a drug is approved pursuant to its own New Drug Application, it is not the same "drug" and thus not a "line extension." The court of appeals disregarded this express statutory definition as "wandering on the periphery." App., *infra*, 21a. The questions presented are:

1. Does a decision that upholds an agency statutory interpretation merely because it is "perfectly sensible" or "reasonable and consistent with the statutory framework" comport with *Loper Bright Enterprises* v. *Raimondo*, 144 S. Ct. 2244 (2024)?

2. Is an agency free to disregard reliance interests engendered by its prior interpretation of the statute it administers simply because that interpretation was announced in a non-binding document like a notice of proposed rulemaking?

CORPORATE DISCLOSURE

Petitioner Vanda Pharmaceuticals Inc. discloses that it has no parent corporation and that BlackRock Fund Advisors owns more than 10% of its stock.

RELATED PROCEEDINGS

Vanda Pharms. Inc. v. *Ctrs. for Medicare & Medicaid Servs.*, No. 23-1457 (4th Cir. Apr. 10, 2024)

Vanda Pharms. Inc. v. *Ctrs. for Medicare & Medicaid Servs.*, No. 22-cv-00977 (D. Md. Mar. 31, 2023)

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PETITION FOR A WRIT OF CERTIORARI

Petitioner Vanda Pharmaceuticals Inc. respectfully petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the Fourth Circuit.

OPINIONS BELOW

The opinion of the court of appeals (App., *infra*., 1a) is reported at 98 F.4th 483. The opinion of the district court (App., *infra*, 29a) is unreported but is available at 2023 WL 2743364.

JURISDICTION

The court of appeals entered its judgment on April 10, 2024. On June 11, 2024, the Chief Justice extended the time for filing this petition to September 6, 2024. This Court's jurisdiction is invoked under 28 U.S.C. § 1254(1).

STATUTORY AND REGULATORY PROVISIONS INVOLVED

42 U.S.C. § 1396r-8(c)(2). App., *infra*, 85a.

42 U.S.C. § 1396r-8(k)(7)(A). App., *infra*, 87a.

42 C.F.R. § 447.502. App., *infra*, 89a.

42 C.F.R. § 447.509(a)(4). App., *infra*, 89a.

STATEMENT

The Medicaid statute requires drug manufacturers to pay rebates to state Medicaid programs; if a manufacturer raises the price of a drug beyond the pace of inflation, a penalty provision greatly enhances the rebate amounts, significantly reducing the Medicaid outlay for the drug. The inflation penalty compares a price metric in the current quarter to the baseline of the same metric at time of launch, adjusted for inflation.

Congress became concerned that a manufacturer could circumvent this penalty provision by making minor changes to a drug and releasing the new version with a new baseline—thus "shedding" the inflation penalty from the original drug by resetting the baseline at a higher level. To close this loophole, Congress adopted the "line extension" provision as part of the Patient Protection and Affordable Care Act, which defines a line extension as a "new formulation." A drug that is deemed a "line extension" is subject to an alternative rebate formula that in effect applies the inflation penalty from the *original* drug to the *line extension*, thereby removing any benefit of the line extension having received a new baseline.

For more than a decade, the Centers for Medicare & Medicaid Services (CMS) construed this statute as it was written and intended: It limited its interpretation of "new formulation" to drugs that reflected merely minor changes to existing drugs.

Recently, however, CMS adopted a regulatory definition of "line extension" that, by the agency's own admission, was "much broader" than its previously published interpretations of the statute. App., *infra*, 17a (quoting *Medicaid Program; Revising Medicaid Drug Rebate Requirements*, 85 Fed. Reg. 37,286, 37,295 (June 19, 2020)). The net effect of the new rule is to declare any new drug which has an active ingredient in common with a prior drug to be a "new formulation," and thus a "line extension," even if the new drug reflects significant changes and innovations.

This new rule has a profound effect on pharmaceutical innovators, like petitioner, that invest enormous sums to create new uses for existing therapeutics that materially improve patients' lives. In reliance

on CMS's previous understanding of the Medicaid statute, Vanda developed Hetlioz LQ®, a liquid formulation of its Hetlioz® product. Hetlioz LQ® is path-breaking in two respects: It is indicated for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome, a rare neurodevelopmental disorder, and it is formulated to be taken by children, dosed according to body weight. Because these are enormous alterations to the original Hetlioz® product, FDA required Vanda to obtain approval via a stand-alone New Drug Application (NDA), rather than the less-onerous supplemental New Drug Application (sNDA). Additionally, Vanda is researching the development of a long-acting injectable (LAI) for its existing product, Fanapt®. Under CMS's old rules, neither of these drugs—both of which are innovative new therapeutics with substantial benefits to patients—would qualify as a "line extension." Now, both do. And, because of the penalty provision, Vanda has no meaningful way to recoup the enormous sums it invested to develop these drugs, which treat disorders that disproportionately burden patients who depend on Medicaid.

Vanda therefore sued to set aside CMS's rulemaking as both contrary to statute and arbitrary and capricious. In rejecting its claims, the court of appeals purported to eschew *Chevron* deference—but in its place applied a form of *Skidmore* deference that threatens to resurrect the now-defunct *Chevron* regime under a different name. Indeed, in response to Vanda's showing that, via a chain of express incorporation, the statutory text establishes a clear limitation governing what may qualify as a line extension—that a drug approved by FDA under a separate NDA is not the same "drug" as the original and thus cannot be a

"line extension"—the court simply brushed off this argument as "invok[ing] provisions that are wandering on the periphery." App., *infra*, 21a. But, in actuality, following those cross-references was the hard but crucial work of interpreting a complicated statute; the statute *mandates* this result. Moreover, in rejecting Vanda's claims challenging CMS's rulemaking as arbitrary and capricious, the court departed from this Court's teachings regarding an agency's responsibilities when it abandons an existing policy for a different one.

If allowed to stand, CMS's re-interpretation threatens the development of innovative new drugs like Fanapt LAI. The extent of the Medicaid rebate burden is critically important for product innovation, as it determines the amounts manufacturers will be able to recoup on their research and development investments. Here, Vanda seeks to innovate to deliver a truly meaningful therapeutic benefit to help schizophrenia patients, a group that disproportionately relies on Medicaid. But because CMS's interpretation will treat Vanda's long-acting injectable as a "line extension" of Fanapt®—notwithstanding the game-changing benefits for medication adherence of a once-a-month injection over a multiple-times-per-day pill—CMS's action puts the financial viability of this innovative treatment, and therefore Vanda's ability to deliver it to patients, at risk.

For each of these reasons, the Court should grant certiorari to reaffirm the critical guardrails to agency power established by judicial exercise of independent judgment on statutory questions as well as the courts' arbitrary-and-capricious review of an agency's change in position. Or, in the alternative, the Court should

grant, vacate, and remand to the court of appeals, which did not have the benefit of *Loper Bright* when it rendered its judgment.

A. Legal background

1. The Medicaid program authorizes federal funding to enable States to provide medical assistance to low-income individuals. 42 U.S.C. § 1396-1; *Pharm. Rsch. & Mfrs. of Am.* v. *Walsh*, 538 U.S. 644, 650 (2003). To reduce Medicaid spending on prescription drugs, Congress amended the Medicaid statute to establish the Medicaid Drug Rebate Program (MDRP). See Omnibus Budget Reconciliation Act of 1990, Pub. L. No. 101-508, § 4401, 104 Stat. 1388, 1388-143 to 1388-161. The MDRP requires drug manufacturers, as a condition of receiving Medicaid payments, to enter into agreements with the Department of Health and Human Services (HHS) to provide rebates on their Medicaid sales of outpatient prescription drugs. 42 U.S.C. § 1396r-8(a)(1); *Pharm. Rsch.*, 538 U.S. at 652.[1]

The rebate amount for a brand-name prescription drug is the sum of two components: the basic rebate, which is generally a minimum of 23.1% of average manufacturer price (AMP)—a metric that already reflects manufacturer commercial discounts, and an additional rebate. The basic rebate ensures that

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[1] Medicaid represents one out of every six dollars spent on healthcare in the United States. Elizabeth Williams, Robin Rudowitz, & Alice Burns, *Medicaid Financing: The Basics*, KFF (Apr. 13, 2023), perma.cc/RQ2D-N9EK. As a result, a substantial proportion of manufacturers participate in Medicaid, and the MDRP "covers a significant portion of drug purchases in the United States." *Astra USA, Inc.* v. *Santa Clara Cnty.*, 563 U.S. 110, 114 (2011).

Medicaid receives a significant discount on the drugs it reimburses. This discount can be higher than 23.1% if the current average manufacturer price is sufficiently greater than the "best" price for the drug—the lowest available price from the manufacturer during the rebate period. 42 U.S.C. § 1396r-8(c)(1).

The additional rebate penalizes increases in the drug's price that outpace inflation.[2] As originally enacted, the additional rebate for each unit of a drug paid for by Medicaid is given by the difference between the drug's AMP for the current rebate period, and the AMP of the drug when it was first marketed (the baseline), adjusted for inflation. 42 U.S.C. § 1396r-8(c)(2)(A). Thus, the additional rebate is designed to force the manufacturer of a drug to reimburse Medicaid for any price increases above the rate of inflation, as measured by reference to the baseline AMP established when the drug entered the market.

As an example, consider a drug with a base-date AMP of $10. Suppose that the inflation-adjusted baseline AMP is $13, but that the drug's current AMP is $40. On top of a basic rebate of at least $9.24 (23.1% of $30, assuming that this minimum rebate amount applies), the drug would incur a $27 additional rebate ($40 minus $13). Thus, the total rebate would be $36.24 ($9.24 plus $27)—a huge discount as compared to the drug's AMP (which already reflects commercial discounts, and is thus lower than the drug's market

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[2] Drug manufacturers will sometimes have legitimate business reasons to increase the price of a drug beyond the inflation rate. For example, if a pre-launch estimate of the market size for a drug turns out to have been overly optimistic, the manufacturer may be required to increase price to recoup the development costs, given smaller than expected sales volumes.

price). This is the penalty imposed on a manufacturer who raises prices faster than inflation.

Rebates are calculated separately "with respect to each dosage form and strength" of a "single source drug" or an "innovator multiple source drug." 42 U.S.C. § 1396r-8(c)(1), (2). A "single source drug" is defined as a "covered outpatient drug" that is "produced or distributed under a new drug application approved by the Food and Drug Administration" (*id*. § 1396r-8(k)(1)(A)(iv)), while an "innovator multiple source drug" is defined as a "covered outpatient drug" that is "marketed under a new drug application approved by the Food and Drug Administration," for which there is at least one generic on the market (*id*. § 1396r-8(k)(1)(A)(i)-(ii)). A "covered outpatient drug" is in turn defined in part as a prescription drug that "is approved for safety and effectiveness as a prescription drug under section 505 * * * of the Federal Food, Drug, and Cosmetic Act"—in other words, which is approved under a New Drug Application. *Id*. § 1396r-8(k)(2)(A); see 21 U.S.C. § 355.

Hence, a distinct additional rebate calculation, and a distinct baseline AMP, applies to each brand-name "drug" that has been approved by the Food and Drug Administration (FDA) under its own New Drug Application—*and* to every "dosage form" (*e.g.*, a pill, a tablet, a capsule, or an injection) and "strength" (*e.g.*, 10 mg vs. 20 mg) of each such "drug."

2. Congress was concerned that this framework could allow a drug manufacturer to circumvent the price-increase penalty by releasing a slightly altered formulation of an existing drug with a different dosage form or strength (say, by switching from a half-strength twice-daily oral tablet to a once-daily tablet),

thereby obtaining a new, higher baseline AMP. This would reset the baseline for purposes of the additional rebate, without providing any meaningful clinical benefit over the existing drug. By replacing the existing drug with the new formulation, the manufacturer not only could escape the inflation penalty on the existing drug, but could even launch the new formulation at a higher price without triggering an additional rebate inflation penalty (because the baseline AMP for the new formulation would reflect its higher launch price).

To take the above example, a manufacturer could release a new dosage form of the drug and price it so that the baseline AMP is $40 (the same as the current AMP of the original drug). Assuming the minimum rebate amount applies, the basic rebate owed would still be $9.24 ($23.1% of $40). But unlike with the original drug, there would be no inflation penalty additional rebate. The new formulation thus incurs a total rebate of only $9.24.

In 2008, a Congressional Budget Office (CBO) report drew attention to this loophole, pointing out that because "new dosages or formulations" created by "modifications to existing drugs" triggered a separate additional rebate calculation with a new baseline AMP, drugmakers could circumvent the additional rebate by making a "slight alteration" or "minor change" to an existing drug product and releasing it as a "new" product at a "substantially higher" price. CBO, Budget Options, Volume I: Health Care 143 (2008) (CBO Report), perma.cc/JUU6-6N4Z.

Congress then focused on this potential strategy by drugmakers. One House committee report noted that "new dosages or formulations" of "existing

drugs"—otherwise referred to as "product line extensions"—were considered new products that incurred a separate rebate calculation. H.R. Rep. No. 111-299, Part 1, at 635 (2009). This allowed drug manufacturers to "set higher prices that will not incur Medicaid's additional rebates" by the simple expedient of "making slight alterations to existing products" and releasing these "new products" at higher prices. *Ibid*. A Senate committee report similarly observed that because "new dosages or formulations" are "considered new products" for purposes of calculating the additional rebate, some drug manufacturers were able to "avoid incurring additional rebate obligations," despite significantly increasing prices, simply by "making slight alterations to existing products, sometimes called line-extensions." S. Rep. No. 111-89, at 92 (2009). These reports shared a common focus on "slight alterations," distinguishing such minor changes from genuine pharmaceutical innovation.

3. To block drug manufacturers from exploiting this loophole to raise prices without incurring additional rebate penalties—and without providing additional clinical benefit to Medicaid patients—Congress adopted the line extension provision.

The Patient Protection and Affordable Care Act, Pub. L. No. 111-148, § 2501(d), 124 Stat. 119, 309 (2010), and subsequent amendments modified the Medicaid statute to impose an alternative rebate calculation on "line extensions." Under this alternative formula, the additional rebate for a line extension is equal to the greater of two amounts. The first is the additional rebate calculated using the usual formula: the difference between the AMP of the line extension for the current rebate period and the line extension's

inflation-adjusted AMP when it was first marketed. 42 U.S.C. § 1396r-8(c)(2)(C)(ii). The second amount is the "highest additional rebate" incurred by "any strength of the original * * * drug," calculated as a percentage of the original drug's AMP, multiplied by the AMP of the line extension. *Id.* § 1396r-8(c)(2)(C)(iii).

In other words, the alternative rebate calculation closes the loophole that previously existed, by applying the additional rebate obligation incurred by the *original* drug to the line extension (unless the line extension's own additional rebate is greater).

Consider our example where an original drug with only a single strength had a baseline AMP of $10—which, adjusted for inflation, is $13. Suppose as before that the AMP of the original drug is now $40. The inflation penalty (additional rebate) for the original drug would be equal to $27 ($40 minus $13). Suppose further that the drug manufacturer now releases a "line extension" of the original drug, with a $60 AMP. The line extension would be subject to a basic rebate of $13.86 (23.1% of $60, assuming the minimum rebate amount applies). Applying the alternative rebate formula (the greater of two amounts) to determine the additional rebate, the first amount (the usual additional rebate formula applied to the line extension) would be zero, because the line extension has not experienced any price increases that outpace inflation. Because the original drug has only one strength, and its additional rebate as a percentage of its AMP is equal to 67.5% ($27 divided by $40), the second amount is $40.50 (67.5% of $60). Since the second amount is obviously greater than the first, the additional rebate on the line extension would equal

$40.50. The total rebate owed on the line extension would therefore equal $54.36 ($13.86 + $40.50)—effectively a more than 90% discount for Medicaid compared to the line extension's AMP.

If the current average price of the original drug matches the release price of the line extension (both are $60), the results are even more dramatic. Again, the line extension would be subject to a basic rebate of at least $13.86 (23.1% of $60). But this time, the additional rebate owed on the line extension would be 78%: $47 ($60 minus $13), divided by the original drug's current AMP of $60. The additional rebate on the line extension is therefore $46.80 (78% of $60). The total rebate calculation for the line extension would thus be $60.66 ($13.86 + $46.80)—*more than* 100% of the current AMP of the line extension. Thus, the line-extension drug would be effectively *free* for Medicaid, despite the fact that the examples above concern only the line extension's initial release price, where, by definition, the line extension's price has not outpaced inflation.

This example also underscores why the panel's assertion below—that "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" (App., *infra*, 25a-26a)—presents an inaccurate picture of the effects of line-extension status on a manufacturer's ability to recoup a drug's development costs. Assuming the same price movements as in the second example above, the rebate percentage owed on the line extension would be at least 101.1% of AMP (a minimum of 23.1% plus 78%), no matter how high the manufacturer sets the initial price of the line-extension drug.

Under the statutory line-extension provision, a drug qualifies as a line-extension—and thus becomes subject to the alternative rebate calculation—when it meets two conditions. *First*, the drug must be a "line extension," defined to mean, "with respect to a [single source or innovator multiple source] drug, a new formulation of the drug, such as an extended release formulation." 42 U.S.C. § 1396r-8(a)(2)(C). *Second*, the drug must not simply be a line extension but a "line extension of a single source drug or an innovator multiple source drug *that is an oral solid dosage form*." *Id*. § 1396r-8(a)(2)(C)(i) (emphasis added).

4. CMS first sought to implement the statutory definition of a "line extension" in 2012, when it published a proposed Covered Outpatient Drugs rule. A "line extension" would be defined as a brand-name drug that "has been approved by the FDA as a change to the initial brand name listed drug" in that it "represents a new version of the previously approved drug," a "new formulation of a previously approved drug," a "new combination of two or more drugs," or a "new indication for an already marketed drug." *Medicaid Program; Covered Outpatient Drugs*, 77 Fed. Reg. 5,318, 5,338 (Feb. 2, 2012). However, a "new strength of the initial brand name drug" would be "exclude[d]" from the definition of a line extension. *Ibid*. CMS also proposed to specify that for the alternative rebate calculation to apply, "both the initial brand name drug and the line extension drug have to be an oral solid dosage form drug." *Ibid*.

When CMS finalized the Covered Outpatient Drugs rule in 2016, it declined to finalize its earlier proposed definition of a "line extension." *Medicaid Program; Covered Outpatient Drugs*, 81 Fed. Reg.

5,170, 5,265 (Feb. 1, 2016). Despite declining to finalize a definition of a "line extension" for purposes of applying the alternative rebate calculation, CMS gave significant indications of its position in the regulatory preamble.

First, it said nothing to contradict its previous announcement that it "believe[d]" the proposed rule "is consistent with * * * the line extension provisions in the Affordable Care Act." 77 Fed. Reg. at 5,338. More, the agency stated that it did not consider "new strength[s] of the same formulation of the initial brand name listed drug" to be a line extension. *Id*. at 5,340. And, in explaining how the alternative rebate is to be calculated, CMS referred repeatedly to a "line extension that is an oral solid dosage form." *Id*. at 5,341.

5. In June 2020, CMS again proposed to define a "line extension." In an about-face from its longstanding position that both the line extension and the original drug must be an oral solid dosage form, CMS now proposed that "only the initial * * * drug"—and not the line extension—"must be an oral solid dosage form." 85 Fed. Reg. at 37,294.

CMS also proposed a new definition of "line extension," recognizing that this definition would interpret the term "more broadly" than it previously had. 85 Fed. Reg. at 37,295. CMS's earlier definition of "line extension" tracked the statutory language, interpreting it as a "new formulation of the [original] drug." *Ibid*. In lieu of that approach, CMS now proposed a "much broader definition of new formulation" than before, defining it to mean "*any* change" to the original drug, including but "not * * * limited to" changes in "dosage form, strength, route of administration,

ingredients, pharmacodynamics, or pharmacokinetic properties," provided only that "the new formulation contains at least one active ingredient in common with the initial brand name listed drug." *Ibid*. This proposed definition swept into "new formulations" changes to the strength of an original drug.

CMS finalized a revised version of its proposed definition of "line extension" in a final rule (Rule) issued on December 31, 2020. See *Medicaid Program; Revising Medicaid Drug Rebate Requirements*, 85 Fed. Reg. 87,000, 87,044 (Dec. 31, 2020) (codified at 42 C.F.R. § 447.502). The finalized definition follows the proposed definition in specifying "line extension" to mean a "new formulation of the [original] drug," and goes on to define "new formulation" in sweeping terms. *Ibid*. Under CMS's unbounded finalized definition, a new formulation encompasses any "change to" the original 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." *Ibid*.

The Rule also finalized CMS's proposal that "only the initial single source drug or innovator multiple source drug" need be "an oral solid dosage form" for the alternative rebate calculation attaching to line extensions to apply, contrary to its prior proposal and interpretation. 85 Fed. Reg. at 87,034.

B. Factual and procedural background

Petitioner Vanda Pharmaceuticals Inc. researches, creates, and brings to market innovative drugs to treat rare disorders. Many of the patients who benefit from Vanda's drugs are Medicaid beneficiaries. The viability of petitioner's research and development program depends to a large degree on

revenue from Medicaid reimbursements. The Rule's expansion of the line extension definition—with its accompanying burdensome alternative rebate obligations—threatens the foundations of Vanda's efforts at developing innovative treatments. Two drugs developed by Vanda, Hetlioz LQ® and Fanapt LAI, demonstrate the risk to pharmaceutical innovation posed by the Rule's overreaching interpretation of the line-extension provision.

1. In 2014, Vanda received FDA approval to market Hetlioz® as the first-ever drug to treat Non-24-Sleep-Wake-Disorder (Non-24), a rare, debilitating circadian rhythm disorder. Based on the success of Hetlioz® in treating Non-24, Vanda studied whether it could be used to treat other conditions that impact circadian rhythms, such as Smith-Magenis Syndrome (SMS), a rare neurodevelopmental disorder. After clinical trials showed significant therapeutic benefits, petitioner obtained FDA approval to market Hetlioz® with an indication for the treatment of sleep disturbances in patients 16 years and older with SMS.

Because individuals with SMS experience sleep disturbances as early as infancy, Vanda also studied how Hetlioz® might benefit a pediatric population. For Hetlioz® to be used in treating children aged below 12, it needed to be in a dosage form that would allow dosing to be calibrated according to each child's body weight. Vanda therefore sought to transform Hetlioz® from an oral solid dosage form (a capsule) into an oral suspension (a liquid). In developing this liquid formulation, Vanda had to ensure that the new drug would have the release and absorption kinetics necessary for it to be effective.

Vanda succeeded in developing Hetlioz LQ®, which has an oral suspension dosage form, to treat children with SMS experiencing sleep disturbances. Recognizing that Hetlioz LQ® was a different drug from Hetlioz®, FDA required Vanda to submit a New Drug Application—rather than only a supplemental New Drug Application—to obtain approval to market Hetlioz LQ®. See 21 C.F.R. § 314.70(h) (providing that a supplemental New Drug Application cannot be used to approve a "different drug"). FDA subsequently approved Hetlioz LQ® to treat sleep disturbances in pediatric SMS patients 3 to 15 years old.

Under CMS's interpretation of the line-extension provision prior to the Rule, Hetlioz LQ® would not have been subject to the alternative rebate calculation that attaches to a "line extension" drug: Hetlioz LQ® has a different strength than Hetlioz® and is not in an oral solid dosage form. But because Hetlioz LQ® is a "change to" Hetlioz®, it falls within CMS's unbounded new definition of "line extension," despite being a different drug than Hetlioz®, approved under a separate NDA and reflecting a very significant change to the original drug—a shift from an oral solid dosage form to an oral suspension, which meets an unmet patient need.

2. Vanda also developed and manufactures Fanapt®, an atypical antipsychotic delivered in tablet form. FDA has approved Fanapt® to treat schizophrenia in adults, as well as episodes associated with bipolar disorder.

Because of the nature of the disorder, which includes symptoms of delusions, hallucinations, and disorganization, schizophrenia patients often struggle to adhere to treatment regimens. See, *e.g.*, Kyoko

Higashi et al., *Medication Adherence in Schizophrenia*, 3 Therapeutic Advances in Psychopharmacology 200 (Aug. 2013), perma.cc/7FUG-4UCV.

To improve patients' medication adherence, Vanda has been working to develop Fanapt LAI, a long-acting injectable version of the drug. Rather than requiring patients to take different doses of tablets multiple times each day, a long-acting injectable enables patients to receive medication through injections given a few times each year. Long-acting injectables like Fanapt LAI therefore promise to revolutionize schizophrenia treatment. See, *e.g.*, C.A. J.A. 641.

Under CMS's longstanding prior interpretation, Fanapt LAI would not have been a "line extension" subject to the more onerous alternative rebate calculation. It is, of course, not an oral solid dosage form and the strength of Fanapt LAI (250-500mg every few months) differs significantly from Fanapt® (12-24mg every day). And more generally, it is far from a slight alteration; it is an innovation that promises significant benefits to patients. But under the Rule, Fanapt LAI qualifies as a line extension because it was developed by making "change[s] to" Fanapt®.

Vanda has already made substantial investments in developing Fanapt LAI, having obtained one patent and filed applications for others relating to this innovative treatment. C.A. J.A. 15-16. The Rule's sweeping new interpretation of the line-extension provision has, however, forced petitioner to reconsider whether to continue investing in the development of Fanapt LAI. C.A. J.A. 27-28. A disproportionately large segment of schizophrenia patients are Medicaid beneficiaries, and Medicaid would therefore account for a large share of Fanapt LAI's expected sales. Because

Fanapt LAI would be subject to the alternative rebate calculation under the Rule, petitioner may be unable to recoup sufficient revenue to bear the enormous costs of further developing Fanapt LAI. *Ibid*.

3. Petitioner brought an action under the Administrative Procedure Act (APA), challenging the Rule's definition of "line extension" as contrary to statute and arbitrary and capricious. On cross-motions for summary judgment, the district court ruled in favor of CMS on all counts, expressly deferring to the agency's views under *Chevron, U.S.A., Inc.* v. *Nat. Res. Def. Council, Inc.*, 467 U.S. 837 (1984).

A panel of the Fourth Circuit affirmed, agreeing with the district court that the Rule's definition of "line extension" is consistent with the Medicaid statute, and that CMS's abrupt re-interpretation of the line-extension provision was not arbitrary and capricious. App., *infra*, 27a-29a.

Although decided before this Court's decision in *Loper Bright*, the court of appeals putatively disavowed any application of the *Chevron* framework, which the agency had declined to invoke on appeal. The panel therefore ostensibly applied only the "traditional tools of statutory interpretation," accepting the agency's views only to the extent that they had the "power to persuade." App., *infra*, 12a (quoting *Skidmore* v. *Swift & Co.*, 323 U.S. 134, 140 (1944)).

The panel nonetheless held that the Rule's definition of a "new formulation," and hence of a "line extension," as any "change to" the original drug was "a perfectly sensible way to implement the regime set by the Medicaid statute." App., *infra,* 13a. Relying on dictionary definitions of the statutory terms "new" and

"formulation," the panel reasoned that a "*different* formula creates a *new* formulation." *Id*. at 14a.

The panel was not persuaded by Vanda's argument that, because the statute defines a line extension as a "new formulation of the" original single source or innovator multiple source "drug," a line extension cannot encompass new drugs so different from their originals that they require a separate NDA for FDA approval. The panel emphasized that the FDA drug approval process has a "different focus" than the MDRP, such that if Congress had intended to tie the definition of a "line extension" to this distinction, it "would have done so explicitly." App., *infra,* 20a.

As for petitioner's claim that CMS's failure to adequately consider drugmakers' reliance on its previous longstanding interpretation was arbitrary and capricious, the panel declared that it was "loath to impose on agencies an obligation to make allowances for industry players who relied on proposals never implemented." App., *infra,* 25a.

REASONS FOR GRANTING THE PETITION

The court of appeals' decision applies the wrong standard, and therefore unsurprisingly reaches the wrong result. Although purporting to apply only *Skidmore* deference, the court in fact upheld the agency's interpretation as merely "reasonable," "sensible," and "consistent with" the statute. Such analysis is inconsistent with federal courts' "responsibility" to "use every tool at their disposal to determine the best reading of the statute," rather than simply "declaring a particular party's reading 'permissible,'" and therefore deferring to it. *Loper Bright Enters.* v. *Raimondo*, 144 S. Ct. 2244, 2266, 2273 (2024). And its analysis

contravenes this Court's precedents on agencies' consideration of reliance interests, too.

Because the decision below threatens to resurrect *Chevron* deference under another name, the Court should grant certiorari to preclude this deviation—and, in so doing, construe a crucially important statutory provision. Alternatively, the Court should grant, vacate, and remand for reconsideration in light of *Loper Bright*.

A. The court of appeals applied an unduly deferential analysis that is inconsistent with *Loper Bright*.

Although it expressly disavowed *Chevron* deference (App., *infra*, 11a), and paid lip service to the "traditional tools of statutory interpretation" (*ibid.*), the court of appeals' interpretive method cannot be squared with the Court's recent reaffirmance that "[c]ourts must exercise their independent judgment in deciding whether an agency has acted within its statutory authority." *Loper Bright*, 144 S. Ct. at 2273. And, by applying an unduly deferential standard, the court reached a substantive result that is at odds with the text and structure of a critically important statute. Each of these failings warrants review.

1. The court of appeals purported to give weight to CMS's interpretative views "only if they have the 'power to persuade,'" invoking this Court's decision in *Skidmore*. App., *infra*, 12a (quoting *Skidmore*, 323 U.S. at 140). But its analysis was in fact more deferential than the Court's precedents allow.

First, the court upheld the agency's interpretation because it found that interpretation merely "'reasonable' and 'consistent with the statutory framework.'"

App., *infra*, 17a-18a (quoting *Fed. Exp. Corp.* v. *Holowecki*, 552 U.S. 389, 402 (2008)); see also *id.* at 13a (upholding interpretation that "strikes us as a *perfectly sensible* way to implement the regime set by the Medicaid statute.") (emphasis added). While that might have been an accurate description of *Skidmore* during the *Chevron* era,[3] it is not consistent with the Court's description of federal courts' role in *Loper Bright*.

There, in the course of overturning *Chevron*, the Court made clear that "statutes, no matter how impenetrable, do—in fact, must—have a single, best meaning. That is the whole point of having written statutes." *Loper Bright*, 144 S. Ct. at 2266. Agency cases are no exception: "In an agency case as in any other, * * * even if some judges might (or might not) consider the statute ambiguous, there is a best reading all the same." *Ibid.*; see also *id.* at 2271 (regardless of how the agency offers an interpretation, "[t]he statute still has a best meaning, necessarily discernible by a court deploying its full interpretive toolkit.")

And it is the court's job to find that single, best meaning: "[I]nstead of declaring a particular party's reading 'permissible'"—as was sufficient for deference under *Chevron*—courts must "use every tool at their disposal to determine the best reading of the statute

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[3] In fact, *Holowecki* found "deference * * * appropriate" only because *both* the agency's interpretation was "reasonable * * * and consistent with the statutory framework," *and* the challenger's contrary position was "in considerable tension with the structure and purposes of" the statute. 552 U.S. at 401. Here, by contrast, the court of appeals seems to have found reasonableness and consistency to be sufficient to defer under *Skidmore*. App., *infra*, 11a-12a.

and resolve the ambiguity." *Loper Bright*, 144 S. Ct. at 2266; see also, *e.g.*, *id.* at 2273 ("[T]he APA bars judges from disregarding th[e] responsibility" to "apply their 'judgment' *independent* of the political branches * * * just because an Executive Branch agency views a statute differently.").

But the standard applied by the court of appeals here, though quoted from a case applying *Skidmore*, functionally resurrects the very analysis the Court put to rest in *Loper Bright*. The panel upheld an agency interpretation because it was "reasonable" and "*consistent with* the statutory framework" (App., *infra*, 17a-18a (emphasis added))—in other words, simply because it was permissible. After *Loper Bright*, that is not the law: "In the business of statutory interpretation, if it is not the best, it is not permissible." 144 S. Ct. at 2266.

Second, even if the court had properly understood the *Skidmore* analysis, the agency interpretation here is not eligible for any deference under the *Skidmore* regime in any event. As the Court has repeatedly explained, "[a]n agency interpretation * * * which conflicts with the agency's earlier interpretation is 'entitled to considerably less deference' than a consistently held agency view." *Good Samaritan Hosp.* v. *Shalala*, 508 U.S. 402, 417 (1993) (quoting *INS* v. *Cardoza-Fonseca*, 480 U.S. 421, 446 n.30 (1987)); see also, *e.g.*, *Holowecki*, 552 U.S. at 399 ("Under *Skidmore*, we consider whether the agency has applied its position with consistency.").

That caveat to *Skidmore* survived *Loper Bright*: While "courts may * * * seek aid from the interpretations of those responsible for implementing particular statutes," only those "interpretations issued

contemporaneously with the statute at issue, *and which have remained consistent over time*," are "especially useful in determining the statute's meaning." *Loper Bright*, 144 S. Ct. at 2262 (citing *Skidmore*, 323 U.S. at 140) (emphasis added).

Here, however, the interpretation to which the court of appeals applied *Skidmore* deference is the furthest thing from longstanding and consistent. As the court itself put it, "[w]hen proposing the regulation at issue here, the agency acknowledged that it had chosen a '*much broader definition* of new formulation' than in previous * * * proposals." App., *infra*, 17a (quoting 85 Fed. Reg. at 37,295) (emphasis added). That is, "[t]he agency 'believe[d] that the statute g[ave] [it] discretion and authority to interpret the term 'line extension' broadly," notwithstanding that "its broadened definition" was contrary to the agency's previous published understanding of the statute. *Ibid.* (quoting 85 Fed. Reg. at 37,295).

Under the Court's longstanding precedents, therefore, *Skidmore* should have been inapplicable. Yet the court of appeals applied it anyway—and in a manner that, as discussed above, threatens to reanimate *Chevron* deference under another name.

2. Because the court of appeals gave undue deference to the agency's interpretation, it reached a result that is at odds with the statute.

The Medicaid statute specifies that "the term 'line extension' means, with respect to *a drug*, a new formulation of *the drug*." 42 U.S.C. § 1396r-8(c)(2)(C) (emphases added). For one product to be a line extension of another product, therefore, the two must be "formulation[s]" of a single drug—"the" drug whose line is being extended. *Ibid.*; see, *e.g.*, *Cochise*

Consultancy, Inc. v. *United States ex rel. Hunt*, 587 U.S. 262, 272 (2019) ("[T]he 'use of the definite article . . . indicates that there is generally only one' person [or thing] covered.") (quoting *Rumsfeld* v. *Padilla*, 542 U.S. 426, 434 (2004)).

And, the line-extension provision itself expressly refers to "a line extension of a *single source drug* or an *innovator multiple source drug*." 42 U.S.C. § 1396r-8(c)(2)(C)(i) (emphases added). Each of these terms is defined by the statute to turn on the existence of "a new drug application approved by the Food and Drug administration." *Id.* § 1396r-8(k)(7)(A)(ii), (iv).[4]

Because a "drug" for purposes of this portion of the Medicaid statute is defined by its FDA-approved New Drug Application, it follows that a new product requiring its own, separate New Drug Application—rather than the less onerous supplemental New Drug Application—cannot be the same "drug" as an existing drug. And because a line extension *must* be the same "drug" as the original product from which it is derived (42 U.S.C. § 1396r-8(c)(2)(C)), a product requiring its own standalone New Drug Application—like Vanda's products Hetlioz LQ® and Fanapt LAI—by definition *cannot* be a line extension.

Indeed, to our knowledge, the only judicial decision to have addressed similar issues adopted exactly that reading of the Medicaid statute. See *Ipsen*

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[4] "'[S]ingle source drug' means a covered outpatient drug * * * which is produced or distributed under a new drug application approved by the Food and Drug Administration." 42 U.S.C. § 1396r-8(k)(7)(A)(iv). "'[I]nnovator multiple source drug' means a multiple source drug that is marketed under a new drug application approved by the Food and Drug Administration." *Id.* § 1396r-8(k)(7)(A)(ii).

Biopharmaceuticals, Inc. v. *Azar*, 2020 WL 3402344, at *10 (D.D.C. June 19, 2020) ("[A] distinct 'drug' for Medicaid rebate purposes is defined by FDA's approval of a distinct [New Drug Application] pursuant to section 505.").[5]

The court of appeals dismissed all of this as a "lengthy chain" of "oblique cross-reference[s]," observing that "the FDA has a different focus from the Medicaid Drug Rebate program." App., *infra*, 20a. True, but irrelevant where the *Medicaid statute*—not the statute administered by the FDA—expressly defines the categories of "drug" involved here by reference to their FDA-approved New Drug Applications. 42 U.S.C. § 1396r-8(k)(7)(A)(ii), (iv). Moreover, the "length[]" of a "chain" of statutory cross-references does nothing to detract from the binding legal authority of each statutory link in that chain. Tracing statutory cross-references that incorporate an express definition *is* the hard work of statutory construction—but the panel below refused to engage in that labor in favor of deference to the agency's preferred construction.

"Well has it been said that Medicaid statutes and regulations 'are among the most completely impenetrable texts within human experience.'" *United States ex rel. Sheldon* v. *Allergan Sales, LLC*, 24 F.4th 340, 352 (4th Cir. 2022) (Wilkinson, J., for the court) (quoting *Rehab. Ass'n of Va., Inc.* v. *Kozlowski*, 42 F.3d 1444, 1450 (4th Cir. 1994)), *vacated on rehearing en banc*, 49 F.4th 873. But as this Court reminded the judiciary in *Loper Bright*, all "statutes, no matter *how*

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[5] *Ipsen Biopharmaceuticals* was briefed extensively below, but the court of appeals did not address it.

impenetrable * * * have a single, best meaning," and it is the courts' task to "use every tool at their disposal to determine [that] best reading." 144 S. Ct. at 2266; cf. *Kisor* v. *Wilkie*, 588 U.S. 558, 575 (2019) ("[A] court cannot wave the ambiguity flag just because it found the regulation impenetrable on first read," even if "[a]gency regulations can sometimes make the eyes glaze over.").

Here, rather than undertake the hard work of grappling with a seemingly impenetrable statute, the court of appeals upheld an agency's newfound interpretation because it was "reasonable" and "consistent with the statutory framework," and seemed "a perfectly sensible way to implement the regime set by the Medicaid statute." App., *infra*, 13a, 17a-18a. Because such analysis runs the risk of resurrecting exactly the kind of deference that *Loper Bright* rejected in favor of "independent legal judgment" (144 S. Ct. at 2266), the Court should grant certiorari.

Alternatively, the Court should grant, vacate, and remand for reconsideration in light of *Loper Bright*, which was issued after the Fourth Circuit's decision here.

B. The court of appeals' rejection of legitimate reliance interests is contrary to this Court's precedents.

The decision below also threatens to undermine another fundamental principle of administrative law: that "[w]hen an agency changes course, * * * it must 'be cognizant that longstanding policies may have engendered serious reliance interests that must be taken into account.'" *DHS* v. *Regents of Univ. of Cal.*, 591 U.S. 1, 30 (2020) (quoting *Encino Motorcars, LLC*

v. *Navarro*, 579 U.S. 211, 221-222 (2016)); see also *id.* at 33 ("[B]ecause DHS was not writing on a blank slate, it was required to assess whether there were reliance interests, determine whether they were significant, and weigh any such interests against competing policy concerns.") (citation and emphasis omitted).

1. As noted, one aspect of the rule challenged here—that drugs in dosage forms other than oral solid can be a line extension—is a complete reversal of the agency's previous statements on the matter. See pages 12-14, *supra*. This is a hugely important change; drug development is a years-long (indeed, often decades-long) process that requires significant investment long before any return is achieved, and manufacturers must forecast the commercial viability of their pipeline products in order to make decisions about which projects to pursue.

The agency's prior position—that non-pill drugs categorically cannot be line extensions—thus led to reasonable reliance throughout the industry, as avoiding line extension status can have significant revenue effects, particularly for drugs used primarily by specialized patient populations eligible for Medicaid. Indeed, Vanda relied on CMS's previous interpretation in devoting resources to developing Fanapt LAI and Hetlioz LQ®, on the understanding that those drugs, because they are an injectable and a liquid, respectively, could not be line extensions. Other manufacturers similarly relied on the agency's representations. See, *e.g.*, Mot. for S.J. at 38-41, *Incyte Corp.* v. *Becerra*, No. 21-cv-3378 (D.D.C.), Dkt. 13-1 (another manufacturer's pending challenge to the same regulation, arguing that it relied on the prior interpretation in developing a new and innovative drug); C.A. J.A. at

562-563, 577, 619, 624, 626 (other manufacturers' comments describing reliance).

Below, the agency did not contend that it had in fact "assess[ed] whether there were reliance interests, determine[d] whether they were significant, and weigh[ed] such interests against competing policy concerns," as the law requires. *Regents*, 591 U.S. at 33; see Gov't C.A. Br. 39-41.[6] Instead, it argued—and the court held—that it did not *need* to consider reliance interests, because the agency's prior interpretation was contained in a notice of proposed rulemaking, and "[w]e are * * * loath to impose on agencies an obligation to make allowances for industry players who relied on proposals never implemented." App., *infra*, 25a.

2. That holding—that an agency policy or interpretation announced in a notice of proposed rulemaking is categorically unable to generate the kind of "legitimate reliance" that an agency must at least consider (*Regents*, 591 U.S. at 30)—is directly contrary to this Court's precedents.

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[6] CMS did contend that it had "accounted for whatever 'legitimate reliance' manufacturers placed on its prior proposals by acknowledging that the finalized rule differed from the 2012 proposal and explaining at length the rationale for the change." Gov't C.A. Br. 40 (citation omitted). But that is plainly insufficient; the requirement for an agency to "display awareness that it is changing position and show that there are good reasons for the new policy" is *separate* from the additional requirement to "be cognizant" of "serious reliance interests that must be taken into account." *Encino Motorcars*, 579 U.S. at 221-222 (quotation marks omitted); see also *Regents*, 591 U.S. at 30-33 (agency action was arbitrary and capricious for failing to consider reliance interests, notwithstanding that the agency acknowledged and explained the reasoning behind its change in position).

For one thing, the Court in *Encino Motorcars* held that an interpretation contained in, among other documents, "a notice of proposed rulemaking" that the agency ultimately did "not proceed[] with" *did* create reliance interests with which the agency had to grapple. 579 U.S. at 217-218, 222-223. That alone renders the court of appeals' seeming per se exclusion of such interpretations contrary to binding precedent.

The court of appeals' decision is also in significant tension with *Regents*. There, in a close parallel to the situation here, the agency argued that it "did not need to" consider reliance interests, because in its view, "disclaimers" in the old policy stating that it "conferred no substantive rights" "automatically preclude[d] reliance interests" in the policy. 591 U.S. at 30-31. The Court emphatically rejected that position, holding that while the circumstances of the prior policy "are surely pertinent to the *strength* of any reliance interests, * * * that consideration" still "must be undertaken by the agency in the first instance." *Id.* at 31; see also *id.* at 32 ("Making that difficult decision"—whether "reliance * * * was unjustified in light of the express limitations" of the prior policy, and if not, whether "other interests and policy concerns outweigh any reliance interests"—"was the agency's job, but the agency failed to do it.").

Regents thus strongly suggests that the requirement to consider reliance interests is not subject to any per se exclusions like that applied by the court of appeals here. Rather, it is "the agency's job" to consider reliance interests "in the first instance, subject to normal APA review"—and any circumstances that might entitle the asserted reliance interests to "diminished weight" must be considered within that analysis

by the agency; they do not "automatically preclude reliance interests." 591 U.S. at 30-32. The court of appeals' per se exclusion of interpretations contained in proposed rules is to the contrary.

3. That bright-line exclusion also makes little sense given the circumstances of this case. As discussed, CMS in 2012 "propose[d] that both the initial brand name drug and the line extension drug have to be an oral solid dosage form drug." 77 Fed. Reg. at 5,338. Not only did it make that policy proposal, but it affirmatively stated that "we believe this policy is consistent with * * * the line extension provisions in the Affordable Care Act." *Ibid.*

In 2016, CMS announced that it had "decided not to finalize the proposed regulatory definition of line extension" "at this time." 81 Fed. Reg. at 5,197, 5,265. But it gave no indication that, as a substantive matter, it no longer "believe[d]" that that definition was "consistent with" the statute, as it had said when proposing it. 77 Fed. Reg. at 5,338. And in the same release, CMS affirmatively directed "manufacturers * * * to rely on the statutory definition of line extension" and to "use reasonable assumptions in their determination whether their drug qualifies as a line extension drug." 81 Fed. Reg. at 5,265.

In other words, this was not simply a policy proposal that was "float[ed]" and then abandoned, as the court of appeals would have it. App., *infra*, 25a. Instead, the agency (1) affirmatively announced that excluding non-pill forms of drugs from the line extension definition was "consistent with" the governing statute; (2) decided not to finalize the rule as a policy matter, but did nothing to undermine its previous interpretive statement; and (3) directed manufacturers to

"rely on the statutory definition of line extension"—the very same definition the agency had *just interpreted* to exclude non-pill drugs.

Under these circumstances, reliance by manufacturers was manifestly reasonable, further underscoring the wisdom of this Court's instruction against per se rules in this context. See *Regents*, 591 U.S. at 30-32. Because the court of appeals' decision departs from this guidance—not to mention that its per se rule conflicts with *Encino Motorcars*—the court should grant review.

C. The questions presented are important.

This case presents a compelling opportunity for the Court to address two important issues that are likely to recur.

1. The Court's decision in *Loper Bright* marked a sea change in its administrative law jurisprudence, discarding four decades of deference to agencies under *Chevron* in favor of a renewed focus on the "independent legal judgment" the Framers expected of the federal courts. *Loper Bright*, 144 S. Ct. at 2266. Unsurprisingly, many jurists supported the *Chevron* regime as both legally correct and a normatively desirable method of "allocating responsibility for statutory construction between courts and agencies." *Id.* at 2294 (Kagan, J., dissenting).

Given this long history of deference, comprising the entire legal career of many if not most current federal judges, it is understandable that even a lower court attempting in good faith to apply this Court's directions could slip back into a deferential posture, even without applying *Chevron* by name. And it is easy to see how the language seized upon by the court

of appeals here—suggesting that deference might be appropriate under *Skidmore* if an agency's interpretation is "reasonable" and "consistent with the statutory framework" (App., *infra*, 17a-18a (quoting *Holowecki*, 552 U.S. at 402))—could metamorphose into exactly the kind of deference regime the Court rejected in *Loper Bright*. See *Loper Bright*, 144 S. Ct. at 2254 (*Chevron* "required courts to defer to 'permissible' agency interpretations * * * even when a reviewing court reads the statute differently.").

Of course, if the lower courts effectively recreate the *Chevron* deference regime by purporting to give *Skidmore* respect to agency views, *Loper Bright*'s express overruling of *Chevron* as inconsistent with the APA's command would be rendered a nullity. It is therefore critical that the Court intervene to reaffirm that—notwithstanding any stray language in its previous *Skidmore* decisions—courts may not uphold agency interpretations without "us[ing] every tool at their disposal to determine the best reading of the statute" and ultimately "apply[ing] their judgment *independent* of the political branches." *Loper Bright*, 144 S. Ct. at 2266, 2273.[7]

2. Similarly important is the obligation of agencies not to reverse course without at least considering the interests of those who may have reasonably relied on the agency's previous positions. Agencies in the modern regulatory state are constantly changing their minds, not least due to their ubiquitous involvement in ideologically charged or politically salient issues, and the attendant change in direction every four or

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[7] Alternatively, as noted above, the Court may simply grant, vacate, and remand in light of *Loper Bright*.

eight years with the changing of presidential administrations. Compare, *e.g.*, Nadia Popovich et al., *The Trump Administration Rolled Back More than 100 Environmental Rules. Here's the Full List*, N.Y. Times (updated Jan. 20, 2021), perma.cc/AD6R-FRZR, with Matthew Daly, *Biden Restores Federal Environmental Regulations Scaled Back by Trump*, PBS News (Apr. 19, 2022), perma.cc/FF4G-4QZ5.

Such changes are the prerogative of each administration, but the APA provides critical protections for the regulated public caught in the bureaucratic whiplash. Indeed, this Court has had to remind agencies, and the lower courts, of their obligations to consider reliance interests on at least three occasions over the past fifteen years. See *Regents*, 591 U.S. at 30-33; *Encino Motorcars*, 579 U.S. at 221-222; *F.C.C.* v. *Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009). Given the critical importance of the protections provided by this doctrine to all those affected by federal administrative action—which is to say, all of us—the Court should not permit decisions like the court of appeals' here to weaken those guardrails.

3. Finally, the importance of the substantive statutory interpretation question here also counsels in favor of certiorari. As petitioner's drugs Hetlioz LQ® and Fanapt LAI demonstrate, innovative new drugs that confer significant patient benefit compared to the status quo are being ensnared by onerous alternative rebates under CMS's overbroad interpretation of the line-extension provision. For innovation to be financially viable, drug manufacturers must be able to recoup the required large upfront investments in research and development by earning sufficient revenues from drug sales. For drugs serving a patient

population whose care is disproportionately covered by Medicaid, the alternative rebate calculation frequently results in rebate amounts that are so onerous as to render drug development commercially unviable, particularly for smaller drug manufacturers. The setback to pharmaceutical innovation from CMS's improper expansion of the line-extension provision ultimately harms patients, especially the vulnerable patient populations that depend on Medicaid.

The line-extension provision, when interpreted in line with Congress's intent, carefully balances the need for pharmaceutical innovation with the goal of controlling drug costs for the Medicaid program. The undisputed purpose of the provision was to close the loophole that previously enabled some drugmakers to circumvent their additional rebate obligations by making slight alterations to their existing drug products and releasing these line extensions with price hikes above the inflation rate. See pages 7-12, *supra.* The line-extension provision achieves this purpose by narrowly targeting the alternative rebate, while leaving genuinely innovative new drugs subject to the less burdensome regular additional rebate calculation.

In upholding the Rule, the court of appeals improperly deferred to what it deemed to be the reasonable "balance struck by the *agency's* * * * regulation between cost control and room for pharmaceutical innovation." App., *infra,* 28a (emphasis added). But the *agency's* balance between achieving cost savings for the Medicaid program and preserving adequate incentives for innovative drug development must be set aside if, as here, it conflicts with the more innovation-protective balance struck by *Congress*. This Court must ensure that Congress's judgment is honored,

and that pharmaceutical innovation is protected against CMS's overreach.

CONCLUSION

The Court should grant the petition. Alternatively, it should grant, vacate, and remand in light of *Loper Bright*.

Respectfully submitted.

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