IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

VANDA PHARMACEUTICALS, INC.,	*	
	*	
Plaintiff,	*	
	*	
v.	*	Civil Action MJM-22-977
	*	
CENTERS FOR MEDICARE & MEDICAID SERVICES, *et al*.,	*	
	*	
Defendants.	*	

* * * * * * * * * * *

MEMORANDUM OPINION

Plaintiff Vanda Pharmaceuticals, Inc. ("Plaintiff" or "Vanda") brings this lawsuit against the Centers for Medicare & Medicaid Services ("CMS") and Chiquita Brooks-LaSure, in her official capacity as Administrator of CMS, (collectively, "Defendants") under the Administrative Procedure Act, 5 U.S.C. § 551 *et seq.* ("APA"), challenging a final rule of CMS ("the Rule") interpreting the "line extension" provision of the Medicaid Drug Rebate Program, 42 U.S.C. § 1396r-8(c)(2)(C).[1] Currently pending are Plaintiff's motion for summary judgment (ECF 17) and Defendants' cross-motion for summary judgment (ECF 26). The Court has reviewed the record, as well as the pleadings and exhibits, and finds that no hearing is necessary. Loc. R. 105.6. For the reasons stated below, Plaintiff's motion will be DENIED, and Defendants' motion will be GRANTED.

I. Background

A. Statutory and Regulatory Framework

CMS is a federal agency under the U.S. Department of Health and Human Services

[1] The parties have consented to proceed before a United States magistrate judge pursuant to 28 U.S.C. § 636(c). ECF 15.

("HHS"). CMS administers the federal Medicaid program, and this case rises from CMS's rulemaking process concerning the Medicaid Drug Rebate Program ("MDRP"). This case also implicates the Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq*. ("FDCA"), which is administered by the Food and Drug Administration ("FDA"), another federal agency under HHS.

1. The Medicaid Drug Rebate Program

Congress created Medicaid in 1965 when it added Title XIX to the Social Security Act. *Pharm. Research & Mfrs. of Am. v. Walsh*, 538 U.S. 644, 650 (2003). It is a cooperative federal-state program through which federal financial assistance is provided to states that reimburse certain medical costs for the needy. *Id*. at 650. In return, participating states must pay a share of the costs and comply with certain federal requirements. The states must have a plan for medical assistance that is approved by CMS. 42 U.S.C. § 1396a. As part of its Medicaid plan, a state may offer optional coverage for prescription drugs. 42 U.S.C. § 1396d(a)(12). All fifty states and the District of Columbia have elected to participate in Medicaid and to include prescription drug coverage in their Medicaid plans.

In 1989, the Senate Special Committee on Aging issued a report on prescription drug prices finding that drug prices were rising far faster than inflation. *United States Senate Special Committee on Aging, Prescription Drug Pricing: Are We Getting Our Money's Worth?* U.S. Government Printing Office (1989), https://www.aging.senate.gov/imo/media/doc/reports/rpt289.pdf. According to the report, rising drug prices, particularly the prices of new drugs, were driving up State Medicaid program costs and putting prescription drug coverage at risk. *Id*. at 1. Congress established MDRP, 42 U.S.C. §

1396r-8, to offset federal and state costs of "covered outpatient drugs"[2] dispensed to Medicaid beneficiaries. *See In re Namenda Direct Purchaser Antitrust Litig*., 331 F. Supp. 3d 152, 193 (S.D.N.Y. 2018).

MDRP requires drug manufacturers to enter into drug rebate agreements with the federal government to provide quarterly rebates to the states on Medicaid sales of their covered outpatient drugs. 42 U.S.C. § 1396r-8(a)(1), (b), (c). Federal payments to each state are accordingly reduced by the rebate amounts states receive from manufacturers. *Id*. This process guarantees to Medicaid "the benefit of the best price" when it comes to paying for prescription drugs. H.R. Rep. No. 101-881, at 96 (1990).

The terms of each Medicaid National Drug Rebate Agreement are set by statute, 42 U.S.C. § 1396r-8(b), and participating manufacturers must pay specified rebates to the states, determined by a formula set forth in § 1396r-8(c). The unit rebate amount, or URA, for each drug purchase by a Medicaid beneficiary is the sum of: (1) the basic rebate; and (2) the additional rebate, if applicable. 42 U.S.C. § 1396r-8(c). Both parts of the rebate are calculated based in part on the "average manufacturer price" ("AMP") of the drug, which is generally defined as the average price paid to the manufacturer for the drug by wholesalers and retail community pharmacies. *Id.* § 1396r-8(k)(1).

The basic rebate for drugs is calculated by multiplying the number of units of each dosage form and strength of the drug paid for under the state plan during the rebate period by the greater of (1) 23.1% of the AMP or (2) the difference between the AMP and the "best price" (which is akin to the lowest price offered) of the drug for the rebate period. *Id.* § 1396r-8(c)(1).

[2] A "covered outpatient drug," is defined, in part, as a drug "which is approved for safety and effectiveness as a prescription drug under section 505 or 507 of the [FDCA] or which is approved under section 505(j) of [the FDCA, 21 U.S.C. § 355]." 42 U.S.C. § 1396r-8(k)(2)(A)(i).

The additional rebate applies when a drug's AMP rises faster than inflation. It is calculated by taking a drug's "Base Date AMP," the drug's AMP during the first full calendar quarter after the product launch and adjusting it for inflation to the current quarter. As such, the additional rebate is the difference between the drug's AMP and Base Date AMP for that quarter. 42 U.S.C. § 1396r-8(c)(2)(A)(ii). In other words, the additional rebate requires manufacturers to rebate the amount that the manufacturer has increased its drug prices beyond the amount necessary to account for inflation. *See id.* § 1396r-8(c)(2). A manufacturer that keeps its drug prices in line with inflation are not required to pay any additional rebate. ECF 26-1 at 1.

2. The Affordable Care Act's Amendments to the Medicaid Statute

For purposes of the inflation-based additional rebate, the Base Date AMP is significant because it is used to calculate the additional rebate due (if any) for the life of each dosage form and strength of a covered outpatient drug. Manufacturers thus had an incentive to create putative "modifications to existing drugs" which were considered "new" products for purposes of seeking new base dates in order to avoid paying some or all of the additional rebate. *See* H. Rep. No. 111-299, Pt. 1, at 635 (2009). When these "new" products were released, manufacturers were able to "set their base period [AMP] to any price, so they are able to set new higher prices that will not incur Medicaid's additional rebates." *Id*.

To curtail this practice, as part of the Affordable Care Act, Congress amended the Medicaid rebate statute to establish an alternative rebate formula for any "drug that is a line extension of a single source drug or an innovator multiple source drug that is an oral solid dosage form." Section 2501(d) of the Patient Protection and Affordable Care Act (Pub. L. 111-148, enacted March 23, 2010), as amended by section 1206 of the Health Care and Education Reconciliation Act of 2010 (Pub. L. 111-152, enacted March 30, 2010) (collectively referred to as the Affordable Care Act).

"[T]he term 'line extension' means, with respect to a drug, a new formulation of the drug, such as an extended release formulation." Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111-152, § 1206, 124 Stat. 1029, 1057–58 (codified at 42 U.S.C. § 1396r-8(c)(2)(C)). As relevant here, "[t]he term 'single source drug' means a covered outpatient drug ... which is produced or distributed under a new drug application approved by the [FDA]," 42 U.S.C. § 1396r-8(k)(7)(iv), and "[t]he term 'innovator multiple source drug' means a multiple source drug that is marketed under a new drug application approved by the [FDA]," 42 U.S.C. § 1396r-8(k)(7)(ii). "The term 'multiple source drug' means, with respect to a rebate period, a covered outpatient drug ...." 42 U.S.C. § 1396r-8(k)(7)(i). Congress did not define the term "new formulation."

Under the line extension provision, a manufacturer must compare the total rebate amount under the standard rebate calculation of a line extension to the "alternative" rebate amount for the line extension, and the greater of two is the line extension drug's total unit rebate amount. 42 U.S.C. § 1396r-8(c)(2)(C)(i); Compl. ¶ 52. The alternative rebate formula is found at 42 U.S.C. § 1396r-8(c)(2)(C)(iii)(I) through (III).[3] The alternative rebate formula results in a higher rebate amount only when the original drug's cost outpaces inflation. ECF 26-1 at 11. If the original drug's price does not increase faster than the rate of inflation, then the alternative calculation for the line extension would not produce a higher rebate amount than the standard rebate amount. *Id.*

Section 1396r-8(c)(2)(C) of the Act was further amended by section 705 of the Comprehensive Addiction and Recovery Act of 2016 ("CARA") (Pub. L. 114-198, enacted July 22, 2016) to exclude from the definition of line extension an abuse deterrent formulation of the drug. As such, "the term 'line extension' means, with respect to a drug, a new formulation of the

[3] CMS has provided detailed explanation, illustrations, and examples of the calculation of rebates for a line extension drug. *See Medicaid Program; Covered Outpatient Drug; Line Extension Definition; and Change to the Rebate Calculation for Line Extension Drugs*, 84 Fed. Reg. 12,130, 12,133–34 (Apr. 1, 2019).

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." 42 U.S.C. § 1396r-8(c)(2)(C). Abuse-deterrent formulations ("ADF") of prescription drugs were exempted from the definition of "line extension" when calculating Medicaid rebates in order to "incentivize the development of ADF to combat opioid abuse." H.R. Rep. No. 114-559, at 3 (2016).

3. CMS's Rulemakings and the Challenged Rule

a. Proposed Definition of "Line Extension" in 2012

During its Covered Outpatient Drug ("COD") rulemaking in 2012, CMS proposed a definition of "line extension":

> Line extension means a single source or innovator multiple source drug that is in an oral solid dosage form 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 listed drug, such as a new ester, a new salt, or other noncovalent derivative; 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, 5,360 (Feb. 2, 2012). CMS also stated:

> For the purpose of calculating the unit rebate amount under the Affordable Care Act, we propose that both the initial brand name drug and the line extension drug have to be an oral solid dosage form drug. We also propose to exclude a new strength of the initial brand name drug from the definition of a line extension drug. We have adopted this policy in order to capture all new formulations (including extended release formulations) and potential line extensions of single source or innovator multiple source drugs. Further, we believe this policy is consistent with our understanding of the line extension provisions in the Affordable Care Act.

Id. at 5,338.

CMS discussed the issue of identifying the line extension of the initial brand name listed drug:

> We have determined that we do not have the ability to identify the line extension of the initial brand name listed drug based on manufacturer rebate submissions. We consulted with the FDA to determine if the FDA currently keeps a list of line extension drugs as we have defined the term, and the FDA does not.
> ….
> We plan to identify line extension drugs by using drug information that is publicly available on the FDA Web sites. As stated, CMS currently does not have the ability to identify whether a drug is a line extension and which drug is the initial brand name listed drug of the line extension drug based on manufacturers' MDRP submissions. Therefore, we plan to rely on drug information obtained from the FDA.

Id. at 5,339. Based on the analysis of the FDA's drug information and data files, CMS proposed to use FDA's assigned Chemical Types 2, 3, 4, and 6 ("new ester, new salt, or other noncovalent derivative," "new formulation," "new combination," and "new indication," respectively) to identify line extension drugs and Chemical Type 1 ("new molecular entity (NME)") to identify an initial brand name listed drug. *Id*. CMS reasoned:

> The FDA classifies all NDAs based on Chemical Type. One measure of innovation is the newness of the listed drug or the drug's active ingredient. The Chemical Type may identify the drug as new, or as related to the active ingredient of another drug that has already been approved.
> . . . .
>
> Chemical Type 2 (new ester, new salt, or other noncovalent derivative) represents the incorporation of different salts or esters, or other noncovalent derivatives (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance of an approved pharmaceutical ingredient into a marketed dosage form which represents a change to the listed drug (21 CFR 314.108(a)). We propose to identify this Chemical Type as a line extension because it describes a new version of the initial brand name listed drug.
>
> Chemical Type 3 (new formulation of a previously approved drug) (not a new salt or new molecular entity) represents a change in the inactive ingredients (excipients) in a drug but no change in the amount of active ingredient. A new formulation may be a dosage form that contains the same active ingredient as was previously approved in a different dosage form as the initial brand name listed.
>
> Chemical Type 4 (new combination) represents a drug comprised of two or more components that are physically, chemically, or otherwise combined or mixed to produce a single drug product. We propose to identify this Chemical Type as a line

> extension because the new combination of the initial brand name listed drug of two or more active ingredients represents a new formulation of the initial brand name listed drugs that are combined to form one drug product.
>
> Chemical Type 6 (new indication for an already marketed drug) represents a change in the description of use of an already marketed initial brand name listed drug in the prevention, treatment, or diagnosis of a recognized disease or condition. According to the National Institute for Health Care Management, research performed on drugs that are already on the market may reveal that they provide safe and effective treatments for diseases or conditions other than the indication(s) for which the product was originally approved. We propose to identify this Chemical Type as a line extension because there is an approval for a new indication that represents a change to the initial brand name listed drug.
>
> Chemical Type 1 (new molecular entity) represents an active ingredient that has never before been marketed in the United States in any form. CMS proposes to use this Chemical Type to identify the initial brand name listed drug of a line extension.

Id. CMS also explained why other Chemical Types 5, 7 and 8 ("new manufacturer," "drug already marketed, but without an approved new drug application (NDA)," and "OTC (over-the-counter) switch," respectively) were not considered line extension drugs. *Id*.

CMS then discussed five criteria that it believed must be met in order to identify line extension drugs and track back to the initial brand name listed drugs using the FDA's drug information:

> First, the line extension drug should be a single source drug or innovator multiple source drug. Manufacturers are already required to report to CMS if their nine-digit NDC drug is a single source drug, innovator multiple source drug, or non-innovator multiple source drug; therefore, we have the information to make this determination.
>
> Second, the line extension drug has to be an oral solid dosage form of a single source drug or innovator multiple source drug in accordance with the definition of an oral solid dosage form previously provided.
>
> Third, the line extension is identified based on Drugs@FDA's application file. Since we currently do not have the ability to identify whether the drug is the actual line extension of the initial brand name listed drug based on manufacturers' submissions, we propose to rely on the FDA's list of Chemical Types to identify which drug is a line extension drug, as described above. Because we do not approve new drugs or changes to a drug, using the Chemical Types would permit us to

> identify line extension drugs based on FDA data, since the FDA currently has an identifier for the Chemical Types in their Drugs@FDA's application file.
>
> Fourth, the initial brand name listed drug of the line extension drug needs to be identified to calculate the Affordable Care Act unit rebate amount for the line extension drug. Again, as described above, we plan to use Chemical Type 1 to assist us in tracking back to the initial brand name listed drug of the line extension drug….
>
> Lastly, CMS currently collects drug product and pricing information by NDC, not by active ingredient. However, the FDA information is mainly available by active ingredient. Therefore, we need to identify the line extension drugs by NDC.

Id. at 5,339–40. The last criterion involved proposed manual matching of Drugs@FDA's application file, the FDA's Orange Book's product file, and the FDA's National Drug Code ("NDC") Directory's application and listing files to obtain relevant information. *Id*.

CMS explained why it proposed exclusion of "new strength[s]" of a drug from the definition of a line extension:

> Additionally, as mentioned in the definition of a line extension drug, we propose that a new strength of the initial brand name listed drug would not qualify as a line extension drug. Furthermore, if we were to consider a new strength to be a line extension, it would be difficult to identify the first strength of the initial brand name listed drug because multiple strengths are often launched simultaneously and CMS would not be able to track back to the first strength of the initial brand name listed drug.

Id. at 5,340.

The Covered Outpatient Drug rulemaking was finalized in 2016, but the proposed definition of "line extension" was not included. *Medicaid Program; Covered Outpatient Drugs*, 81 Fed. Reg. 5,170, 5,197 (Feb. 1, 2016). Nonetheless, CMS summarized the proposed rule to include the plan to use FDA's assigned Chemical Types to identify line extension drugs and initial brand name listed drugs.[4] *Id*. at 5,265. CMS explained that "[s]ince the writing of the proposed rule, FDA has changed the assigned numbers and meaning of some of the Chemical Types." *Id*.

[4] CMS also mentioned the proposed exclusion of a new strength of the initial brand name listed drug from the definition of a line extension drug. 81 Fed. Reg. at 5,265.

CMS then went on to summarize some of the comments it had received and announced that "at this time, we have decided not to finalize the proposed definitions of line extension drug." *Id*. CMS stated:

> Although we are taking into consideration the comments we received on the proposed rule [], we are requesting additional comments on the definition of line extension drug and the identification of new formulations as we may consider addressing these in future rule making. Therefore, at this time, manufacturers are to rely on the statutory definition of line extension at section 1927(c)(2)(C) of the [Social Security] Act, and where appropriate, are permitted to use reasonable assumptions in their determination of whether their drug qualifies as a line extension drug.

Id. The proposed definition of "line extension" was again not included in regulations implementing a technical correction in 2019. *See Medicaid Program; Covered Outpatient Drug; Line Extension Definition; and Change to the Rebate Calculation for Line Extension Drugs*, 84 Fed. Reg. 12,130, 12,132 (Apr. 1, 2019). CMS explained its decision not to finalize a definition of line extension at the time:

> As discussed in the COD final rule, we decided not to finalize the proposed regulatory definition of line extension drug [] and, instead, we requested additional comments on the definition of line extension drug noting that we may consider addressing this issue in future rulemaking (81 FR 5297). After the additional public comment period closed, CARA passed, and we issued guidance to the public on how we would apply section 1927(c)(2)(C) of the [Social Security] Act. While the additional comments that we received through the additional public comment period were insightful of the public's thoughts at a particular time, the comments are not informed by the current statutory framework. Therefore, we are not finalizing a definition of line extension in this final rule and interim final rule with comment period, but instead, are reiterating guidance provided in the COD final rule that manufacturers are to rely on the statutory definition of line extension at section 1927(c)(2)(C) of the [Social Security] Act, and where appropriate are permitted to use reasonable assumptions in their determination of whether their drug qualifies as a line extension drug (81 FR 5265). Reasonable assumptions must be consistent with the purpose of section 1927 of the [Social Security] Act, federal regulations, and the terms of the [Medicaid Drug Rebate] agreement; manufacturers must maintain adequate documentation explaining any such assumptions (83 FR 12770, 12785 (March 23, 2018)). If we later decide to develop a regulatory definition of line extension drug, we will do so through our established Administrative Procedures Act (APA) compliant rulemaking process and issue a proposed rule.

Id.

b. The Challenged Rule

On June 19, 2020, CMS proposed the Rule challenged here. *See Medicaid Program*, 85 Fed. Reg. 37,286 (June 19, 2020). CMS explained the impetus for the proposed rule:

> [W]e proposed to define line extension in the February 2, 2012 proposed rule, but did not finalize a definition in the COD final rule or the April 1, 2019 final rule. We reiterated in the April 1, 2019 final rule that manufacturers are to rely on the statutory definition of line extension at section 1927(c)(2)(C) of the [Social Security] Act, and where appropriate are permitted to use reasonable assumptions in their determination of whether their drug qualifies as a line extension….
>
> After several years of experience with manufacturers self-reporting their line extensions, and numerous inquiries from manufacturers regarding the identification of drugs as line extensions, we have noted inconsistency among manufacturers in their identification of drugs as line extensions. In addition, we are concerned that manufacturers may have a financial incentive to be underinclusive in their identification of drugs as line extensions because a drug identified as a line extension may be subject to a higher rebate. We note that if manufacturers underreport their line extensions, rebates may be calculated incorrectly and underpaid.
>
> We believe the line extension provision was codified in statute to assure that manufacturers are not circumventing rebate liability by creating a line extension drug and avoiding inflation-based additional rebates. In order to ensure that section 1927(c)(2)(C) of the [Social Security] Act is fully implemented and the universe of line extensions is identified consistent with our understanding of Congressional intent, we are proposing to provide further interpretation of the statute in this proposed rule.

Id. at 37,294.

As an initial matter, CMS proposed that "only the initial single source drug or innovator multiple source drug (the initial brand name listed drug) must be an oral solid dosage form." *Id*. CMS acknowledged that in 2012, it was proposed "that both the initial brand name drug and the line extension drug had to be an oral solid dosage form." *Id*. But CMS "did not finalize a regulatory definition of line extension, and instructed manufacturers to make 'reasonable assumptions'

regarding whether a drug is a line extension." *Id*. CMS further explained:

> Upon further evaluation of this statutory language, we believe that the statutory text can be reasonably construed to provide that only the initial single source drug or innovator multiple source drug must be an oral solid dosage form. We believe this interpretation is appropriate because the alternative construction (requiring both the line extension and the initial single source drug or innovator multiple source drug to be an oral solid dosage form) may inappropriately limit the universe of line extension drugs in a manner which would allow a manufacturer to circumvent rebate liability when creating a line extension and to potentially avoid inflation-based additional rebates, in cases where such rebates should apply. Therefore, we are proposing that when determining whether a drug is a line extension, only the initial single source drug or innovator multiple source drug must be an oral solid dosage form. That is, we are proposing that the line extension of the initial brand name listed drug does not need to be an oral solid dosage form. We believe this is consistent with the statutory language and will assist in appropriately identifying drugs that may be line extension drugs.

Id. CMS next proposed to define "line extension" and "new formulation" at 42 C.F.R. § 447.502. Specifically, CMS proposed to define "line extension" to mean, "for a drug, a new formulation of the drug, but … not includ[ing] an abuse deterrent formulation of the drug (as determined by the Secretary)." *Medicaid Program*, 85 Fed. Reg. 37,295. Additionally, CMS proposed to define the term "new formulation":

> [W]e are proposing to define "new formulation" to mean, for a drug, any change to the drug, provided that the new formulation contains at least one active ingredient in common with the initial brand name listed drug. New formulations, (for the purpose of determining if a drug is a line extension) would not include abuse deterrent formulations but would include, but would not be limited to: [e]xtended release formulations[]; changes in dosage form, strength, route of administration, ingredients, pharmacodynamics, or pharmacokinetic properties; changes in indication accompanied by marketing as a separately identifiable drug (for example, a different NDC); and combination drugs, such as a drug that is a combination of two or more drugs or a drug that is a combination of a drug and a device.

Id. "Based on the definition of line extension that was included in the Affordable Care Act," CMS believed that the "statute gives us discretion and authority to interpret the term 'line extension' broadly." *Id*. As to new strengths, CMS noted that "[t]he statutory definition of line extension does

not expressly exclude a new strength of a drug, and we believe a change in strength is a relatively simple modification to a currently marketed product." *Id*. Therefore, the proposed definition of new formulation included changes in strength. *Id.* at 37,296. CMS requested comments on all aspects of the proposed rule, including its proposed definitions of "line extension" and "new formulation," and "specifically on whether these terms should be interpreted more narrowly." *Id*. at 37,295.

On December 31, 2020, the final Rule was published, adopting many of the proposals in the Notice of Proposed Rule, with modifications. 85 Fed. Reg. 87,000. CMS codified a regulatory definition of "line extension" that mirrors the statutory definition and the proposed definition, to mean "a new formulation of the drug but does not include an abuse-deterrent formulation of the drug (as determined by the Secretary)." 42 C.F.R. § 447.502 (85 Fed. Reg. 87,034, 87,101). It defined "new formulation" as "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*. CMS also finalized its proposed interpretation of line extension such that only the initial drug, but not the new formulation, must be in an oral solid dosage form. 85 Fed. Reg. at 87,045.

In finalizing the Rule, CMS responded to comments it had received including, as relevant here, issues concerning the interpretation of "line extension" related to "oral solid dosage form" as well as the definitions of "line extension" and "new formulation" *See id*. at 87,033–45.

With respect to the interpretation of line extension such that "only the initial brand name listed drug must be an oral solid dosage form," several commenters expressed their disagreement:

> [T]hey claimed that the proposal does not align with Congressional intent. They stated that the legislative history shows that Congress intended that the line extension provision applies only to drugs that were "slight alterations" of the previous drug, and that a change from an oral solid dosage form to a different

> dosage form is a significant alteration. A few commenters stated that if the change requires submission of clinical data to FDA, it would be a significant alteration. Some commenters, in discussing fixed-dose combination tablets in treating diseases such as HIV, noted that innovations that improve patient compliance provide significant improvements that benefit patients.

Id. at 87,033. CMS believed that the "proposal is consistent with section 1927(c)(2)(C) of the [Social Security] Act":

> [T]he statute does not require that in order for a drug to be a line extension, the change to a drug must be a slight alteration. Had Congress intended to limit the definition of line extension to only those drugs for which a slight alteration had been made, we believe they would have included that requirement in the statute. Notably, the example of a new formulation that Congress provided in the statute is "an extended release formulation." The change from an immediate release formulation to an extended release formulation may be considered more than a slight alteration. We agree with commenters that innovations that improve patient compliance provide significant improvements that benefit patients and believe this may include extended release formulations. Had Congress intended to limit the line extension provisions to drugs that were only slight alterations, we believe they would have provided an example of a less significant change than "an extended release formulation."

Id.

A few commenters stated that this interpretation "does not align with the statute." *Id*. They argued that "in the statutory language, in the case of 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, Congress plainly intended for the phrase 'that is an oral solid dosage form' to modify the term 'line extension,'" and "because Congress directly addressed this issue, the agency lacks discretion to define ''line extensions'' to include products that are not oral solid dosage forms." *Id*. CMS disagreed with this reading of the statutory text. *Id*. Rather, it believed that "the statutory text can be reasonably construed to provide that only the initial single source drug or innovator multiple source drug must be an oral solid dosage." *Id*. "Although the structure of the sentence does not make it clear which subject is modified by 'that is an oral solid dosage form,'" CMS believed that "the better reading

is that the phrase modifies 'a single source drug or an innovator multiple source drug' because it appears directly following that subject." *Id*. at 87,033–34.

Some commenters stated that CMS's interpretation "is contrary to prior guidance and that the existing interpretation is more reasonable and should be retained." *Id*. at 87,034. CMS did not agree that the proposal was less reasonable than the interpretation discussed in the COD final rule in 2012:

> We acknowledge that in the February 2, 2012 proposed rule, we proposed that both the initial brand name listed drug and the drug that is a line extension were required to be an oral solid dosage form in order for the alternative rebate calculation to be required. However, that proposal was not finalized in the COD final rule. Instead, we stated that we will continue to consider the issues and may consider addressing the issues in future rulemaking (81 FR 5265). We are doing so in this final rule. After consideration of public comments, we are finalizing our proposal that only the initial single source drug or innovator multiple source drug be an oral solid dosage form when determining whether a drug is a line extension. ….
> [W]e are finalizing that the definitions of line extension, new formulation, and oral solid dosage form, as well as the requirement that only the initial brand name listed drug must be an oral solid dosage form, are effective beginning on January 1, 2022. For prior periods, manufacturers should continue to rely on the statutory definition of line extension and may continue to make reasonable assumptions to determine whether their drug is a line extension.

Id.

With respect to the definitions of "line extension" and "new formulation," CMS received "many comments that provided general support for our proposed definition of new formulation." *Id*. Commenters noted that "the proposed definition will help ensure that manufacturers identify all their drugs that are line extensions and will prevent manufacturers from circumventing inflation-based rebates." *Id*. CMS also received many comments concerning various issues, such as those related to statutory concerns, congressional intent, prior guidance and effect on innovation. *See id*. at 87,033–45.

"[M]any comments stat[ed] that the proposed definition of new formulation exceeds

statutory authority because it is too broad or exceeds what Congress authorized." *Id*. at 87,035. Moreover, "[a] few commenters stated that CMS exceeds reasonable statutory interpretation by including several product categories clearly not within the common understanding of new formulation."[5] *Id*. CMS disagreed, reasoning:

> The statute does not define new formulation and it provides only one example of a new formulation, that is, an extended release formulation. The example provided does not expressly limit the types of new formulations that are to be treated as line extensions; rather, using the term "such as," Congress provided one example of a new formulation. Had Congress intended to limit the definition to certain types of changes to a drug, it could have done so in the statute….
>
> We do not believe that the language Congress selected limits the definition of new formulation to include only an extended release formulation of the original drug or a change that is closely related to an extended release formulation. Congress merely provided one example of a new formulation, that is, an extended release formulation.

Id.

CMS also received related comments concerning the intent of Congress and the legislative history. Some commenters stated that "Congressional intent was to capture slight alterations of existing drugs and the legislative history mandates a narrow reading of the statute." *Id*. One argued that "the legislative history makes it clear that a new formulation is only a slight alteration in an existing drug where no additional studies are required by FDA but the proposed definition captures more than slight alterations." *Id*. Other commenters stated that "Congress did not intend to include innovative products and new formulations that provide significant benefits to patients in the definition of line extension." *Id*. CMS reasoned that the line extension is not limited to slight alterations:

> We are aware that there have been discussions about slight alterations made to a

[5] Addressing comments on the proposed use of the phrase "any change" being inconsistent with the statute, CMS stated that the "phrase was followed by specific inclusions and exclusions so that the final definition did not state that any change to a drug qualified the drug as a new formulation." *Id*. at 87,035. However, the definition in the final Rule does not contain that phrase. *Id*.

> drug and those alterations permitted a manufacturer to mitigate the effect of inflation-base[d] rebates on the original drug, however, Congress chose not to include that language, or any similar language, when constructing the statutory language. Additionally, Congress did choose to include an example of one change that is a new formulation. The example given is an extended release formulation, which in general is a change to a drug for which FDA requires additional studies and may be considered a significant change to an original drug. Had Congress intended that the change be slight in order to be considered a new formulation, it could have stated so. The change from an immediate release drug to an extended release drug is not a slight change; there may be significantly different technology involved. Therefore, as Congress had considered slight alterations to a drug in their discussions of line extensions, but chose not to include that limitation in statute, and, as Congress ultimately included a more complex change (that is, an extended release formulation) as an example of a new formulation, we believe that section 1927(c)(2)(C) of the Act is not limited to only slight alterations.
>
> Similarly, Congress could have included language that excluded new formulations that were innovative or provided significant benefits to patients. However, not only was such language not included in the statute, but the only example of a new formulation that was provided (that is, extended release formulation) can provide significant benefits to patients.

Id. at 87,035–36.

Some parts of the proposed definition of new formulation differed from prior guidance. One commenter argued that, for a long time, manufacturers have been relying on prior guidance that "both the original drug and the line extension drug must be an oral solid dosage form for the application of the alternative rebate formula." *Id*. at 87,035–36. "The commenter stated that the prior guidance is reasonable and appropriate." *Id*. at 87,036. Moreover, in the COD final rule, CMS stated that a new strength is not a line extension. *Id*. A few commenters stated that CMS's "reversal of that position is being done without adequate justification and is arbitrary and capricious" because "prior guidance instructed manufacturers to rely on the statutory definition to determine if a drug is a line extension and that some may have assumed that a new strength is not a line extension. *Id*. CMS addressed the reliance issue as follows:

> In the COD final rule, we advised that we were not finalizing a definition of line extension at that time and we reiterated that manufacturers are to rely on the

> statutory definition of line extension and where appropriate are permitted to use reasonable assumptions in their determination of whether their drug qualifies as a line extension drug. We also stated that if we later decide to develop a regulatory definition of line extension drug, we will do so through our established Administrative Procedures Act compliant process and issue a proposed rule. We have done so by issuing the June 2020 proposed rule and this final rule. We have 10 years' experience with various aspects of the line extension provisions that were enacted in the Affordable Care Act and are using our experience to develop a definition of new formulation that we believe is supported by the statute, and supports the MDRP. We do not believe that any changes we have made to prior guidance conflict with the statute or are unreasonable or unjustified in light of the proposed changes.

Id.

CMS received many comments addressing the effect that the proposed definition of new formulation would have on innovation. Some were supportive of the proposed definitions, while others thought that it would have a negative effect on innovation by discouraging, disincentivizing, or penalizing innovation:

> One commenter stated that the proposed definition could make innovation financially untenable for manufacturers. Several commenters discussed that reducing incentives for innovation, research and development, which are long-term, high-risk and expensive investments, will affect clinical outcomes. A few commenters expressed concern that the proposed definition will stifle the development of new and innovative therapies with particular concern for drugs that treat rare diseases. One commenter stated that the proposed definition distorts incentives to innovate because new active ingredients would be incented over other changes, even though new uses, dosage forms, and combination drugs require significant innovation and may lead to important advancements. Several commenters stated that the proposed definition undermines, or is inconsistent with FDA policies and incentives that encourage innovation.

Id. at 87,037. CMS disagreed that the definition of new formulation penalizes innovation:

> If the alternative calculation for a drug that is a line extension results in a higher URA than the standard rebate calculation, it is because the original drug was subject to inflation-based penalties. Therefore, the most important variable that determines if the applicable URA is based on the alternative rebate calculation, rather than the standard calculation, is whether the original drug increased faster than the rate of inflation. The perceived "penalty" for a drug that is a line extension is not a penalty on the new drug, rather it is a continuation of the "penalty" on the original drug. We agree that the treatment of a line extension drug may result in a URA that is

> greater than the standard rebate amount, however we do not believe that this treatment would prevent a manufacturer from pursuing innovation. The fact that the innovation may lead to a higher rebate obligation for a drug that is a line extension is not the result of the innovation. Manufacturers will continue to have incentives to innovate based on multiple factors, as noted in the previous response to a comment. In addition to previously described factors, we understand various FDA policies encourage innovation. We do not believe the proposed definition of new formulation changes those FDA policies and incentives.

Id.

The Rule went into effect on January 1, 2022, and was codified as 42 C.F.R. § 447.502.

4. The Food, Drug, and Cosmetic Act

The FDCA sets forth various requirements for the approval of new drugs. It defines "new drug," in relevant part, to mean "[a]ny drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof." 21 U.S.C. § 321(p). The FDCA then imposes a general requirement that "[n]o person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug." 21 U.S.C. § 355(a).

Section 505(b) provides that persons seeking approval of such new drugs "may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a)." 21 U.S.C. § 355(b)(1). Any such application must contain various pieces of information specified by statute, including, for example, "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use," "a full list of the articles used as components of such drug," and "a full statement of the composition of such drug." 21 U.S.C. § 355(b)(1)(A), (b)(1)(B), (b)(1)(C).

An application submitted under section 505(b)(1) of the FDCA is referred to as a "new

drug application" (or "NDA"). 21 C.F.R. § 314.3. The FDCA's implementing regulations provide, in 21 C.F.R. § 314.50, extensive requirements beyond those imposed in the statute itself that the drug must meet to obtain FDA approval. *See id.* The regulations also define "new drug application" as "the application described under § 314.50, including all amendments and supplements to the application." 21 C.F.R. § 314.3.

The implementing regulations establish a separate process that applies when a manufacturer wishes to make "[s]upplements and other changes to an approved NDA." 21 C.F.R. § 314.70. Under that process, "the applicant must notify FDA about each change in each condition established in an approved NDA beyond the variations already provided for in the NDA," and must "describe the change fully." 21 C.F.R. § 314.70(a).

Certain changes to an approved NDA require the manufacturer to submit a "supplemental new drug application" (or "sNDA") and obtain FDA's approval of that supplemental new drug application "prior to distribution of the product made using the change." 21 C.F.R. § 314.70(b). The supplemental new drug application process is set forth in the FDA's regulations. *See* 21 C.F.R. §§ 314.70–71. Those regulations permit drug manufacturers to give the FDA notice of certain permissible changes to the drug from what was originally submitted in the NDA. 21 C.F.R. § 314.70(a)(1)(i).

In 1983, Congress enacted the Orphan Drug Act to provide pharmaceutical companies with benefits to incentivize the development of "orphan drugs"—that is, drugs that treat rare diseases. *See Spectrum Pharm., Inc. v. Burwell*, 824 F.3d 1062, 1064 (D.C. Cir. 2016). One of those benefits, typically referred to as "orphan-drug exclusivity," is a seven-year period during which the FDA may not approve any other manufacturer's application to market the same drug to treat the same rare disease. 21 U.S.C. § 360cc(a).

The FDCA was amended by the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch–Waxman Amendments"), where Congress established an expedited process for obtaining approval for generic drugs, but, at the same time, provided increased intellectual property rights and periods of market exclusivity for those pioneer manufacturers that invent new drugs. *See*, *e.g.*, *Otsuka Pharm. Co. v. Price*, 869 F.3d 987, 990 (D.C. Cir. 2017). "Once the drug is approved, it is referred to as a 'listed drug.'" *Sanofi–Aventis U.S. LLC v. FDA*, 842 F. Supp. 2d 195, 196–98 (D.D.C.2012) (citing 21 C.F.R. § 314.3(b)). The FDA publishes listed drugs in the "Orange Book," which includes information about applicable patents and periods of exclusivity. *AstraZeneca Pharms. LP v. Food & Drug Admin.*, 872 F. Supp. 2d 60, 62–63 (D.D.C. 2012), *aff'd*, 713 F.3d 1134 (D.C. Cir. 2013)

The FDCA does not contain a definition for "line extension" or "new formulation." ECF 26-1 at 15.

B. Vanda's Development of Hetlioz LQ and Fanapt LAI

Vanda creates, studies, and manufactures innovative drugs to treat rare disorders. Many patients who benefit from Vanda's life-improving drugs receive assistance for their healthcare needs through the Medicaid program. Compl. ¶¶ 3, 78.

In 2014, Vanda brought to market Hetlioz, the first ever drug indicated to treat Non-24-Sleep-Wake-Disorder ("Non-24"), a rare sleep disorder. Compl. ¶¶ 24–25. Non-24 is a disorder in which the body is unable to synchronize its internal circadian rhythm—the process that regulates the sleep-wake cycle—with the 24-hour day. Compl. ¶ 24. Desynchronization of the day-night cycle "can be debilitating." *Id*. Over time, the symptoms of chronic sleep deprivation accumulate, making it difficult for patients to maintain any semblance of a normal life.

Based on the success of Hetlioz in treating Non-24, Vanda began to study whether it could

be modified to treat other conditions that impact circadian rhythms, such as Smith-Magenis Syndrome ("SMS"), a rare neurodevelopmental disorder. Compl. ¶ 26. One of the most common symptoms of SMS is severe sleep disturbances, a chronic problem that develops as early as infancy and continues throughout childhood and adulthood. Compl. ¶ 26. Vanda developed and conducted a clinical trial to study the use of Hetlioz in adult patients with SMS, and patients receiving Hetlioz saw significant improvements in sleep quality and duration. Compl. ¶ 27. Today, Hetlioz bears an indication for the treatment of sleep disturbances in patients 16 years and older with SMS. Compl. ¶ 30.

Vanda then worked on a new product, Hetlioz LQ, in an oral suspension form (a liquid) to treat children with SMS experiencing sleep disturbances. Vanda submitted an NDA seeking FDA approval of Hetlioz LQ, as well as an sNDA to expand the indication of the capsule form of Hetlioz to treat adults with SMS. Compl. ¶ 29. FDA approved Hetlioz LQ on December 1, 2020, for the treatment of sleep disturbances in pediatric SMS patients 3 to 15 years old. Compl. ¶ 30. Vanda alleges that because Hetlioz LQ falls within CMS's definition of "line extension," it has to calculate alternative, higher rebates for Hetlioz LQ. According to Vanda, under CMS's earlier proposal in 2012, Hetlioz LQ would not have been considered a line extension. Compl. ¶¶ 63–64.

Vanda also developed and manufactures Fanapt, an atypical antipsychotic, to treat schizophrenia in adults. Fanapt helps patients suffering from schizophrenia, particularly those who have not benefitted from other therapies, think more clearly, feel less nervous, and experience fewer hallucinations. Compl. ¶ 32. In its current form, Fanapt is a tablet available at various doses ranging from one to twelve milligrams. Compl. ¶ 33. Individuals with schizophrenia often struggle to adhere to treatment regimens. Compl. ¶ 34. That poses a challenge for patients treating with Fanapt, who cannot safely reap all of its benefits until the dose is appropriately titrated. Compl. ¶

33. This process requires daily adjustment of doses the first few weeks a patient begins taking the drug, and ultimately, patients must continue to take the drug twice daily. Compl. ¶ 33. Compliance with taking the right amount of the drug at the right time, without missing doses, is therefore essential for patients on Fanapt.

Vanda has been working to transform the current version of Fanapt into a long-acting injectable formulation, Fanapt LAI. Rather than requiring patients to take different doses of tablets multiple times each day, a long-acting injectable requires patients to receive an injection only a few times each *year*. Thus, the dose for Fanapt LAI (250 to 500 mg every few months) differs significantly from Fanapt (12 to 24 mg every day). Compl. ¶ 35. According to Vanda, long-acting injectable therapeutics would revolutionize schizophrenia treatment. Compl. ¶ 10.

Vanda has made substantial investments in developing Fanapt LAI. It has obtained one patent for it and has also filed and plans to file additional patent applications related to this innovative formulation. Compl. ¶ 37. After years of costly research and development, Vanda began its first pharmacokinetic study for Fanapt LAI in 2018, which is still ongoing and will inform the dosing for a later phase III study on efficacy. Compl. ¶ 38.

According to Vanda, Medicaid beneficiaries make up a disproportionately large segment of Fanapt users. Compl. ¶ 78. Roughly two-thirds of patients with schizophrenia are covered by Medicaid, meaning Medicaid reimbursements comprise an outsized amount of the revenue for Fanapt. Compl. ¶ 78. Vanda alleges that under CMS's 2012 proposal, Fanapt LAI would not have been a "line extension." Vanda claims that it needs to invest millions of more dollars to conduct the necessary clinical studies for approval, but if Fanapt LAI is a line extension, Vanda may not be able to recoup that investment. Compl. ¶ 38.

C. Procedural History

Plaintiff filed this case on April 21, 2022, alleging that (1) the Rule violates the APA because the agency action was not in accordance with the law (Count One); (2) the Rule is arbitrary and capricious (Count Two); and (3) Defendants did not follow the APA's procedural requirements by failing to "address essential considerations" (Count Three). *See* Compl. ¶¶ 97-113. Plaintiff moved for summary judgment (ECF 17), and Defendants opposed Plaintiff's motion and cross-moved for summary judgment (ECF 26).

II. Judicial Review of Agency Action

Under the APA, a reviewing court shall "hold unlawful and set aside" any aspect of a final agency action that is "arbitrary [and] capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). In a case involving review of a final agency action under the APA, summary judgment "serves as the mechanism for deciding, as a matter of law, whether the agency action is supported by the administrative record and otherwise consistent with the APA standard of review." *Sierra Club v. Mainella*, 459 F. Supp. 2d 76, 90 (D.D.C. 2006). In other words, "the entire case ... is a question of law[,]" and the district court "sits as an appellate tribunal." *Am. Biosci., Inc. v. Thompson*, 269 F.3d 1077, 1083 (D.C. Cir. 2001) (footnote and internal quotation marks omitted). The "focal point for judicial review" of agency action "should be the administrative record already in existence, not some new record made initially in the reviewing court." *Camp v. Pitts*, 411 U.S. 138, 142 (1973). And courts "must engage in a searching and careful inquiry of the administrative record, so that we may consider whether the agency considered the relevant factors and whether a clear error of judgment was made." *Casa de Maryland v. Dep't of Homeland Sec*., 924 F.3d 684, 703 (4th Cir. 2019) (alterations and internal quotation marks omitted). The party challenging an agency's action as arbitrary and capricious bears the burden of proof. *Pierce v. SEC*, 786 F.3d 1027, 1035 (D.C. Cir. 2015).

III. Analysis

The relevant text of the Affordable Care Act includes the following:

(1) "In the case of 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, the rebate obligation for a rebate period with respect to such drug under this subsection shall be the greater of the amount described in clause (ii) for such drug or the amount described in clause (iii) for such drug." 42 U.S.C. § 1396r-8(c)(2)(C);

(2) "[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" 42 U.S.C. § 1396r-8(c)(2)(C);

(3) "The term 'single source drug' means a covered outpatient drug…," 42 U.S.C. § 1396r-8(k)(7); and

(4) "The term 'innovator multiple source drug' means a multiple source drug that is marketed under a new drug application approved by the Food and Drug Administration," *Id*.

The pertinent part of the Rule reads:

(1) 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).

(2) 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.

42 C.F.R. § 447.502. Moreover, under CMS's interpretation of line extension, only the initial drug must be in an oral solid dosage form, not the new formulation. 85 Fed. Reg. at 87,045.

Vanda argues that the Rule is contrary to law and in excess of statutory authority. It also argues that the Rule is arbitrary and capricious. Vanda further argues that Defendants did not follow the APA's procedural requirements by failing to "address essential considerations." The Court will consider each of these arguments in turn.

A. Statutory Authority

When a challenger asserts that an agency action conflicts with the language of a statute the

agency administers, a reviewing court applies the two-step framework articulated in *Chevron, U.S.A., Inc. v. Nat. Res. Def. Council, Inc*., 467 U.S. 837 (1984), to determine whether an agency "has stayed within the bounds of its statutory authority" when issuing an action. *City of Arlington v. FCC*, 569 U.S. 290, 297 (2013) (emphasis omitted); *see PETA v. U.S. Dep't of Agric*., 861 F.3d 502, 506 (4th Cir. 2017). First, the court applies ordinary tools of statutory construction to determine "whether Congress has directly spoken to the precise question at issue." *Chevron*, 467 U.S. at 842; *see City of Arlington*, 569 U.S. at 296. If so, and "the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842–43; *see City of Arlington*, 569 U.S. at 296. "[I]f the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843. At this step, the "reviewing court must respect the agency's construction of the statute so long as it is permissible." *FDA v. Brown & Williamson Tobacco Corp*., 529 U.S. 120, 132 (2000); *see also Dada v. Mukasey*, 554 U.S. 1, 29 n.1 (2008) (observing that an "agency need not adopt ... the best reading of the statute, but merely one that is permissible").

Vanda first avers that the Rule overrides Congress's clear policy goals, contradicts the statutory text, and therefore exceeds CMS's statutory authority. Specifically, Vanda argues that (1) a new and distinct drug (a product that requires FDA approval of an NDA) cannot be a line extension of a preexisting drug; (2) a line extension must be an oral solid dosage form; (3) the plain meaning of the term "line extension" should not be overlooked; and (4) "such as an extended release formulation" demonstrates the kind of change that Congress had in mind—which is "a simple one, not a major one requiring FDA approval of an NDA." ECF 27 at 19. Vanda also argues that the Rule is not consistent with the purpose and history of the statute.

The analysis begins with the relevant statutory text: "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," and "the term 'line extension' means, with respect to a drug, a new formulation of the drug, such as an extended release formulation." 42 U.S.C. § 1396r-8(c)(2)(C). "The term 'single source drug' means a covered outpatient drug," and a "covered outpatient drug," is defined, in part, as a drug "which is approved for safety and effectiveness as a prescription drug under section 505 or 507 of the [FDCA] or which is approved under section 505(j) of such Act," 42 U.S.C. §§ 1396r-8(k)(2), 1396r-8(k)(7). An application submitted under section 505(b)(1) of the FDCA is referred to as an NDA. 21 C.F.R. § 314.3. Thus, a single source drug can be a drug product approved under section 505 or 507 of the FDCA via an NDA. Additionally, "'innovator multiple source drug' means a multiple source drug that is marketed under a new drug application approved by the Food and Drug Administration." 42 U.S.C. §1396r-8(k)(7). Therefore, both forms of the original drugs can be a new drug product in that an NDA was required for its FDA approval.

CMS points out that "line extensions (like other drugs) generally must be 'covered outpatient drugs' in order for the [MDRP]to apply to them." ECF 28 at 8. Because a "covered outpatient drug" can be a drug "which is approved for safety and effectiveness as a prescription drug under section 505 or 507 of the [FDCA] or which is approved under section 505(j) of such Act," 42 U.S.C. §§ 1396r-8(k)(2), the intent of Congress is clear that a line extension can be a new drug product with FDA approval. Even if the statute were deemed silent or not unambiguous with respect to this issue, CMS's reading would be "a permissible construction of the statute" because it is based on the general understanding that line extensions (like other drugs) must be "covered outpatient drugs" under MDRP. *Chevron*, 467 U.S. at 843.

Vanda next argues that the clause "that is an oral solid dosage form" in 42 U.S.C. § 1396r-

8(c)(2)(C) modifies "a single source drug or an innovator multiple source drug" as well as "a line extension." CMS argues that the clause "that is an oral solid dosage form" modifies "a single source drug or an innovator multiple source drug" but not "a line extension." CMS avers that its interpretation comports with the rule of the last antecedent, a tool of statutory construction. *See e.g.*, *Lockhart v. United States*, 577 U.S. 347, 351 (2016); *Paroline v. United States*, 572 U.S. 434, 447 (2014); *Barnhart v. Thomas*, 540 U.S. 20, 26 (2003). The *Lockhart* Court explained "[w]hen this Court has interpreted statutes that include a list of terms or phrases followed by a limiting clause, we have typically applied an interpretive strategy called the 'rule of the last antecedent.'" 577 U.S. at 351. The rule provides that "a limiting clause or phrase ... should ordinarily be read as modifying only the noun or phrase that it immediately follows." *Id*. "The rule reflects the basic intuition that when a modifier appears at the end of a list, it is easier to apply that modifier only to the item directly before it." *Id*. "That is particularly true where it takes more than a little mental energy to process the individual entries in the list, making it a heavy lift to carry the modifier across them all." *Id*. The *Lockhart* Court continued:

> For example, imagine you are the general manager of the Yankees and you are rounding out your 2016 roster. You tell your scouts to find a defensive catcher, a quick-footed shortstop, or a pitcher from last year's World Champion Kansas City Royals. It would be natural for your scouts to confine their search for a pitcher to last year's championship team, but to look more broadly for catchers and shortstops.

Id. at 351–52. But "structural or contextual evidence may 'rebut the last antecedent inference.'" *Id*. at 355 (citing *Jama v. Immigration and Customs Enforcement*, 543 U.S. 335, 344, n. 4 (2005)). As the *Lockhart* Court further explained:

> For instance, take "'the laws, the treaties, and the constitution of the United States.'" []. A reader intuitively applies "of the United States" to "the laws," "the treaties" and "the constitution" because (among other things) laws, treaties, and the constitution are often cited together, because readers are used to seeing "of the United States" modify each of them, and because *the listed items are simple and*

parallel without unexpected internal modifiers or structure….

Id. at 352 (emphasis added).

Citing *United States v. Bass*, and other cases including *Lockhart*, Vanda argues that in this case, "[s]ince [the phrase] undeniably applies to at least one antecedent, and since it makes sense with all three, the more plausible construction here is that it in fact applies to all three." ECF 17-1 at 25 (quoting 404 U.S. 336, 339–40 (1971)). *Bass* concerns Title VII of the Omnibus Crime Control and Safe Streets Act of 1968, 18 U.S.C.App. s 1202(a). In pertinent part, that statute reads:

> Any person who—
> (1) has been convicted by a court of the United States or of a State or any political subdivision thereof of a felony . . . and who receives, possesses, or transports in commerce or affecting commerce . . . any firearm shall be fined not more than $10,000 or imprisoned for not more than two years, or both.

Bass, 404 U.S. at 339. "The critical textual question is whether the statutory phrase 'in commerce or affecting commerce' applies to 'possesses' and 'receives' as well as to 'transports.'" *Id*. "Since 'in commerce or affecting commerce' undeniably applies to at least one antecedent, and since it makes sense with all three, the more plausible construction here is that it in fact applies to all three." *Id*. at 339–40.

The Court notes that the relevant cases cited by both sides involve lists of grammatically parallel items without internal modifiers or structure, and with a modifier appearing after the last item. *See Lockhart*, 577 U.S. at 351–52 ("the laws, the treaties, and the constitution of the United States"); *Bass*, 404 U.S. at 339 ("receives, possesses, or transports in commerce or affecting commerce"). In this case, the three items identified by Vanda in the statutory text in question are "a line extension," "a single source drug," and "an innovator multiple source drug." Unlike the terms in the cases cited by the parties, the three items here are not grammatically parallel because the text in question includes internal modifiers. Specifically, "a single source drug" and "an

innovator multiple source drug" are two parallel items that modify "a line extension." And at the end of the two-item list is the final modifier: "that is an oral solid dosage form." Applying the rule of the last antecedent, the phrase "that is an oral solid dosage form" would only apply to "an innovator multiple source drug." Under *Bass* and related cases cited by Vanda, "that is an oral solid dosage form" would apply to both "a single source drug" and "an innovator multiple source drug"—which consistent with CMS's interpretation of 42 U.S.C. § 1396r-8(c)(2)(C). No rule of statutory construction referenced by the parties would support the interpretation suggested by Vanda that the phrase "that is an oral solid dosage form" modifies "a line extension," "a single source drug," and "an innovator multiple source drug."

Even if the structure of the sentence left unclear which antecedent phrase is modified by "that is an oral solid dosage form," and the statute was deemed ambiguous with respect to this issue, then "the analysis shifts to *Chevron* step two, where 'the question for the court is whether the agency's answer is based on a permissible construction of the statute.'" ECF 28 at 9 (quoting *City of Arlington v. FCC*, 569 U.S. 290, 296 (2013)). As discussed above, CMS's interpretation is permissible as it is consistent with a rule of statutory interpretation discussed and applied by the Supreme Court. *See*, *e.g.*, *Lockhart*, 577 U.S. at 351–52.

Third, Vanda argues that the Rule is incompatible with the ordinary dictionary meaning of the words "line" and "extension." Vanda cites *Wisconsin Cent. Ltd. v. United States*, to support an interpretation of "line extension" that results from combining the selected dictionary definitions for "line" and "extension." 138 S. Ct. 2067, 2074 (2018). It is a "fundamental canon of statutory construction" that words generally should be "interpreted as taking their ordinary, contemporary, common meaning ... at the time Congress enacted the statute." *Id*. The Supreme Court explained that "Congress alone has the institutional competence, democratic legitimacy, and (most

importantly) constitutional authority to revise statutes in light of new social problems and preferences. Until it exercises that power, the people may rely on the original meaning of the written law." *Id*. In other words, "[u]nless otherwise defined, statutory terms are generally interpreted in accordance with their ordinary meaning." *BP Am. Prod. Co. v. Burton*, 549 U.S. 84, 91 (2006) (citing *Perrin v. United States*, 444 U.S. 37, 42 (1979)). Here, like other relevant terms of art, such as "single source drug" and "innovator multiple source drug," "line extension" was expressly defined in the statute: "the term 'line extension' means, with respect to a drug, a new formulation of the drug, such as an extended release formulation…." 42 U.S.C. § 1396r-8(k)(7). Because Congress has exercised its constitutional authority to define the term "line extension," a specific concept relevant to understanding the MDRP, it would not be appropriate to attempt to derive the meaning of the term ("line extension") from dictionary definitions of each word that comprises the term.

Vanda further argues that CMS's interpretation of "line extension" is too broad because it captures more than "slight alterations" to existing drugs. Vanda reasons that the example expressly identified by Congress, "such as an extended release formulation," "demonstrates the general kind of change that Congress had in mind—and that kind of change is a simple one, not a major one requiring FDA approval of an NDA." ECF 27 at 19. A premise of Vanda's argument is that "an extended release formulation" is a simple change or slight alteration of an existing drug, and not a major change requiring FDA approval of an NDA. But the change from an immediate release drug to an extended release drug is not necessarily a slight change as "there may be significantly different technology involved." 85 Fed. Reg. at 87,036. Indeed, as CMS pointed out, Vanda's long-acting injectable formulation, Fanapt LAI, an extended release formulation of its atypical antipsychotic medication, Fanapt, appears to involve significantly different technology. According

to Vanda, instead of taking different doses of Fanapt multiple times each day, a long-acting injectable allows patients to receive an injection only a few times each year. Compl. ¶ 35. Vanda states that its long-acting injectable therapeutics "would revolutionize schizophrenia treatment" and has "obtained one patent for it and has also filed and plans on filing additional patent applications related to this innovative formulation." Compl. ¶¶ 35, 37. Moreover, the record does not appear to include any statutory references concerning of FDA approval status of an extended release formulation. Even if the statute is deemed silent, or ambiguous with respect to the example identified by Congress ("an extended release formulation"), Vanda fails to demonstrate that the Rule is unreasonably broad.

Next, Vanda argues that the Rule is inconsistent with the purpose and history of the statute. Vanda argues that "Congress did not intend the line-extension provision to apply broadly" because "the line-extension provision was designed to close the 'loophole' through which some drugmakers circumvented inflation-related rebate payments by making meaningless modifications to existing drugs." ECF 27 at 21. And Congress was also aware of one potential "drawback to [enacting the line extension provision] is that it could discourage some manufacturers from developing new formulations." ECF 27 at 21. The Court notes that both parties cite a report by the Congressional Budget Office ("CBO") published in 2008 (the "CBO Report"). CBO, *Budget Options, Volume I: Health Care*, at 143 (Dec. 2008), https://bit.ly/3w58xGq. The CBO Report highlighted the importance of addressing health care issues to close the nation's fiscal gap:

> Addressing health care issues will be crucial to closing the nation's looming fiscal gap—which is caused to a great extent by rising health care costs. Spending on health care has consumed an ever-increasing share of gross domestic product (GDP) over the past 45 years, and its share will continue to rise unless changes occur to slow the trajectory []. If tax revenues as a share of GDP remain at current levels, additional spending for Medicare, Medicaid, and Social Security will eventually cause future budget deficits to become unsustainable.

Id. at 1. The report presented "a compendium of budget options to help inform federal lawmakers about the implications of various policy choices." *Id.* One of the options provided in the CBO Report concerned applying the Medicaid additional rebate to new formulations of existing drugs:

> Currently, modifications to existing drugs—new dosages or formulations—are generally considered new products for purposes of reporting AMPs to CMS. As a result, drugmakers can often avoid incurring an additional rebate obligation by making a slight alteration to an existing product.
>
> This option would treat a certain type of new formulation—specifically, extended-release versions—of existing drugs more like the original product for purposes of calculating the additional rebate…. Implementing the option would increase rebate amounts and reduce federal outlays….
>
> An advantage of this option is that it would remove a loophole that enables drug manufacturers to circumvent their rebate obligations simply by altering an existing product. Under current law, even a minor change to an existing drug can lead to a "new" product designation that does not trigger the inflation-related rebate even if the initial price for that new product is substantially higher than the price for the original formulation.
>
> A potential drawback to this option is that it could discourage some manufacturers from developing new formulations even when the new products might offer advantages over older versions of the same product.

Id. at 143.

While the CBO Report informed Congress about the loophole through which drug companies circumvented the existing rebate program and the potential risk of discouraging innovation, it was mainly concerned about increasing health care spending, its impact on budget deficits, and mechanisms to reduce health care spending. CBO Report at 1. And the option regarding the Medicaid additional rebate is one of over one hundred options presented for reducing federal spending on health care. *Id.* Additionally, by CBO's assessment, this option "would increase rebate amounts and reduce federal outlays" over one billion dollars over time. *Id.* at 143. The CBO Report echoed a 1989 report of the Senate Special Committee on Aging that warned of the effects of high drug prices on the cost of Medicaid programs. Thus, a narrow interpretation of

the line extension, restricting it to only slight alterations, as Vanda suggests, would not be consistent with the purpose and history of the statute.

Vanda relies on the 2016 amendment that excluded ADF from the definition of line extension to support its argument. However, the 2016 amendment was a correction of "unintended consequences" and part of the efforts to incentivize the development of ADF to combat opioid abuse. H.R. Rep. No. 101-881, at 96. Moreover, instead of modifying or further limiting the scope of the definition of line extension, Congress only exempted ADF from the definition. Had Congress wanted to limit or modify the scope of the line extension definition to address issues such as encouraging innovation, it could have amended the statue accordingly.

Lastly, CMS points out that Congress recently passed legislation with identically worded statutory language in the Inflation Reduction Act of 2022 creating an inflation-based rebate scheme for Medicare Part D ("Part D Rebate Program"). Citing *Lorillard v. Pons*, 434 U.S. 575, 580 (1978), CMS argues that this is "compelling evidence that, contrary to Vanda's arguments, Congress is aware of CMS's treatment of line extensions and approves." ECF 26 at 31.

Twenty months after CMS enacted the challenged Rule, in August 2022, Congress passed the Inflation Reduction Act. *See* Inflation Reduction Act of 2022, Pub. L. No. 117-169, (codified as amended at 42 U.S.C. § 1395w-114(b)(5)(B)). With respect to the "line extension" for purposes of the Part D Rebate Program, the Act provides:

> (B) Treatment of new formulations
>
> (i) In general
> In the case of a part D rebatable drug[6] that is a line extension of a part D rebatable drug that is an oral solid dosage form, the Secretary shall establish a formula for determining the rebate amount under paragraph (1) and the inflation adjusted payment amount under paragraph (3) with respect to such part D rebatable drug and

[6] As relevant here, "the term 'part D rebatable drug' means, with respect to an applicable period, a drug or biological ... that is a covered part D drug (as such term is defined under section 1395w–102(e) of this title)." 42 U.S.C. § 1395w-114b(g)(1)(A).

> an applicable period, consistent with the formula applied under subsection (c)(2)(C) of section 1396r–8 of this title for determining a rebate obligation for a rebate period under such section.
>
> (ii) Line extension defined
> In this subparagraph, the term "line extension" means, with respect to a part D rebatable 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.

42 U.S.C. § 1395w-114(b)(5)(B). Referencing the Affordable Care Act, Congress used a near identical description and definition of "line extension." *Id*. And similarly, Congress did not define the term "new formulation." Moreover, Congress requires the Secretary of HHS to establish a rebate formula, consistent with the line extension alternative rebate formula under the MDRP. 42 U.S.C. § 1395w-114(b)(5)(B)(i).

Vanda argues that the Part D Rebate Program has no bearing on the analysis because "the *Lorillard* canon applies only 'when *judicial* interpretations have *settled* the meaning of an existing statutory provision.'" ECF 27 at 24 (citing *Pareja v. Attorney General*, 615 F.3d 180, 194 n.7 (3d Cir. 2010) (quoting *Merrill Lynch, Pierce, Fenner & Smith Inc. v. Dabit*, 547 U.S. 71, 85 (2006) (emphasis added)); *see also Fogerty v. Fantasy, Inc.*, 510 U.S. 517, 527–33 (1994)). Vanda also reasons that "Congress did not reenact the provision here, as it did in *Lorillard*." ECF 27 at 24.

In *Lorillard*, the Supreme Court stated:

> Congress is presumed to be aware of an administrative or judicial interpretation of a statute and to adopt that interpretation when it reenacts a statute without change.... So too, where ... Congress adopts a new law incorporating sections of a prior law, Congress normally can be presumed to have had knowledge of the interpretation given to the incorporated law, at least insofar as it affects the new statute.

434 U.S. at 580–81. The *Lorillard* Court did not favor judicial interpretation over administrative interpretation of a statute: "Congress is presumed to be aware of an *administrative* or *judicial interpretation of a statute*…." *Id.* at 580 (emphasis added). The Part D Rebate Program is in the

same title and chapter as the MDRP (§ 1396r–8), and both include near identical description and definition of "line extension." Although the text concerning line extension under Part D Rebate Program does not incorporate relevant text of the MDRP, the former references the latter. And HHS is directed to establish a rebate formula, consistent with the line extension alternative rebate formula applied under the latter. Thus, with respect to line extension, the Part D Rebate Program and the MDRP are related. Therefore, it is reasonable to infer that Congress had knowledge of CMS's interpretation of line extension as defined in § 1396r–8, "at least insofar as it affects the new statute." *Lorillard*, 434 U.S. at 581. As such, Vanda's arguments are unavailing.

B. Arbitrary and Capricious

Unlike step-two review under *Chevron*, "which focuses on whether the agency's interpretation was reasonable, 'arbitrary and capricious' review focuses on the reasonableness of the agency's decisionmaking processes." *Rural Cellular Ass'n v. FCC*, 588 F.3d 1095, 1105 (D.C. Cir. 2009). "The scope of review under the 'arbitrary and capricious' standard is narrow and a court is not to substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983). Indeed, arbitrary and capricious review is "fundamentally deferential—especially with respect to matters relating to an agency's areas of technical expertise." *Fox v. Clinton*, 684 F.3d 67, 75 (D.C. Cir. 2012) (alteration adopted and internal quotation marks omitted).

One of the basic procedural requirements of administrative rulemaking is that an agency must give adequate reasons for its decisions. *Encino Motorcars, LLC v. Navarro*, 579 U.S. 211 (2016). The court must "consider whether the [agency's] decision was based on a consideration of the relevant factors and whether there has been a clear error of judgment." *Id*. (quoting *Bowman Transportation, Inc. v. Arkansas-Best Freight System, Inc*., 419 U.S. 281, 285 (1974)). An

agency's decision will be upheld so long as it provides "an explanation of its decision that includes a rational connection between the facts found and the choice made." *State Farm*, 463 U.S. at 42–43.

"An agency must ... demonstrate the rationality of its decisionmaking process by responding to those comments that are relevant and significant." *Grand Canyon Air Tour Coalition v. FAA*, 154 F.3d 455, 468 (D.C. Cir. 1998). Moreover, "[a]gencies are free to change their existing policies as long as they provide a reasoned explanation for the change. When an agency changes its existing position, it need not always provide a more detailed justification than would suffice for a new policy created on a blank slate.'' *Encino Motorcars*, 136 S. Ct. at 2125 (internal citations and quotation marks omitted). However, a more detailed justification is required where the agency's "new policy rests upon factual findings that contradict those which underlay its prior policy." *FCC v. Fox Television Stations, Inc*., 556 U.S. 502, 515 (2009). "In such cases, it is not that further justification is demanded by the mere fact of policy change; but that a reasoned explanation is needed for disregarding facts and circumstances that underlay or were engendered by the prior policy." *Id*. at 515–16.

In conducting a "arbitrary and capricious" review, a court does "not look at the agency's decision as would a scientist, but as a reviewing court exercising [its] narrowly defined duty of holding agencies to certain minimal standards of rationality." *Am. Trucking Ass'ns v. Fed. Motor Carrier Safety Admin.*, 724 F.3d 243, 249 (D.C. Cir. 2013) (alteration adopted and internal quotation marks omitted). A court "may not supply a reasoned basis for the agency's action that the agency itself has not given." *Bowman Transp., Inc*., 419 U.S. at 285. But an agency's decision need not "be a model of analytic precision to survive a challenge," either. *Dickson v. Sec'y of Def*., 68 F.3d 1396, 1404 (D.C. Cir. 1995). A "decision of less than ideal clarity" will be upheld "if the

agency's path may reasonably be discerned." *State Farm*, 463 U.S. at 43. "But where the agency has failed to provide even that minimal level of analysis, its action is arbitrary and capricious and so cannot carry the force of law." *Encino Motorcars*, 579 U.S. at 221 (citing 5 U.S.C. § 706(2)(A); *State Farm*, 463 U.S. at 42–43).

Vanda argues that the Rule produces inexplicable inconsistencies in application and is internally inconsistent. According to Vanda, the Rule irrationally penalizes transformations *from* an oral solid form but not *to* an oral solid form, and there is no reason to disfavor one direction of transformation over the other. CMS addressed this issue when finalizing the Rule: "the better reading is that the phrase ['that is an oral solid dosage form'] modifies 'a single source drug or an innovator multiple source drug' because it appears directly following that subject." 85 Fed. Reg. at 87,034. As explained above, CMS's interpretation is consistent with rules of grammar and is not unreasonable.

Vanda argues that the Rule also "arbitrarily distinguishes between new products requiring marketing approval based on whether the new treatment has an active ingredient in common with a previously approved drug." ECF 27 at 26. Vanda reasons that, under the Rule, "if FDA approves an NDA for a new product that does not have any active ingredients in common with an existing product, it does not qualify as a 'line extension,' but if FDA approves an NDA for a drug with some active ingredient in common with an existing, approved drug, it does so qualify." *Id*. Therefore, according to Vanda, the Rule "inexplicably penalizes manufacturers that work to develop new effective uses for active ingredients that exist in currently approved products." *Id*. CMS addressed this issue, stating "manufacturers' decisions regarding those drugs to research and market depend on multiple factors, including clinical significance of the drug, prescriber and patient demand, costs of research and development, and possible revenues generated." 85 Fed.

Reg. at 87,036. "Whether the drug is a line extension, which could subject it to the alternative rebate calculation, is only one factor in these decisions." *Id*. Moreover, "[t]he financial effect of the alternative rebate calculation would only be applicable in the Medicaid program[.]" *Id.* For drug products with only limited use in Medicaid, "it will continue to be in the interest of a manufacturer to broaden the use of its existing drugs in the form of line extensions, which will lead to increased revenue for the manufacturer."[7] *Id*. Vanda's argument, therefore, is speculative at best.[8] Accordingly, Vanda fails to show that CMS's interpretation of the line extension provision was arbitrary and capricious.

C. Addressing Essential Issues

Vanda argues that CMS, in finalizing the Rule, failed to address substantial comments pertaining to essential matters. Plaintiff asserts that CMS failed to consider manufacturers' reliance on its prior understanding of the line extension provision. "[T]he mere fact that an agency interpretation contradicts a prior agency position is not fatal." *Smiley v. Citibank (S. Dakota), N.A*., 517 U.S. 735, 742 (1996). "Agencies are free to change their existing policies as long as they provide a reasoned explanation for the change." *Encino Motorcars*, 579 U.S. at 221. The agency

[7] CMS points out that manufacturer's pricing decisions alone are responsible for whether a drug is subject to any inflation-based rebate. If the price of a drug is in line with the rate of inflation, it would not be subject to inflationary-based rebate – or would not be penalized. ECF 28 at 15.

[8] Vanda also argues that "[t]he Rule is internally inconsistent because the final regulatory text conflicts with CMS's stated intent in the Rule's preamble." ECF 27 at 27. Vanda averts that throughout the preamble, CMS explains that it decided to exclude certain drugs from its definition of "new formulation." *Id*. According to Vanda the "final regulatory text defining "new formulation" (42 C.F.R. § 447.502) is inconsistent with CMS's conclusions and purposes in the preamble." *Id*. Vanda claims that "[t]he regulatory text defines "new formulation" as *any* "change to the drug" without any exceptions at all." *Id*. (emphasis original). But the Rule does not include the term "any change." The record also shows that at least some changes were excluded. For example, the Rule does not include "a new indication" or "a new combination," and it does not use the terminology "pharmacodynamics" or "pharmacokinetics" which could "incorporated a broader range of changes than [it] intended." 85 Fed. Reg. at 87,039 & 87,042. CMS discussed the comments concerning these issues and decided not to include that in the final rule. Thus, the Court cannot conclude that the agency's interpretation is irrational based on Vanda's allegations.

"need not demonstrate to [the] court's satisfaction that the reasons for the new policy are better than the reasons for the old one; it suffices that the new policy is permissible under the statute, that there are good reasons for it, and that the agency believes it to be better, which the conscious change of course adequately indicates." *FCC v. Fox Television Stations, Inc*., 556 U.S. 502, 515 (2009).

In any event, Vanda fails to show that "anything which can accurately be described as a change of official agency position has occurred here." *Smiley*, 517 U.S. at 742. The prior "positions" cited by Vanda are merely proposals that were never finalized or officially adopted by CMS.[9] The record is clear that CMS explicitly stated that it "decided not to finalize the proposed definitions of line extension drug" in 2016 and in 2019. 81 Fed. Reg. at 5,265; 84 Fed. Reg. at 12,132. Moreover, CMS repeatedly instructed manufacturers "to rely on the statutory definition of line extension." *Id.* As CMS noted in 2019, if CMS decided to develop a regulatory definition of "line extension," it would do so through its established APA-compliant rulemaking process and issue a proposed rule. 84 Fed. Reg. at 12,132. Thus, CMS cannot be accused of suddenly changing its policy with respect to interpreting line extension, because its interpretation of line extension was not finalized until 2020.[10] Manufacturers were notified about the status of the proposals and possible future rulemaking process, and they were repeatedly advised to rely on the statutory language. CMS is not responsible for any manufacturer's reliance on draft proposals. Furthermore, the Rule does not apply retroactively. The Rule was finalized on December 31, 2020. Until these

[9] None of the cases cited by Vanda concern a party's reliance on a proposed rule which was not finalized.

[10] The Court also notes that the earlier proposal of the line extension appears to be broader in scope in certain areas. For example, under the 2012 proposed rule, new indication for an already marketed drug and new combination of the initial brand name listed drug of two or more active ingredients would be a line extension. 77 Fed. Reg. at 5,339. The interpretation of line extension in the final Rule does not include those two categories. 85 Fed. Reg. at 87,039.

specific provisions went into effect on January 1, 2022, manufacturers were given time to evaluate their options and adjust their understanding of what was considered a "new formulation" and thereby a line extension. Therefore, Vanda's argument is not persuasive.

Vanda lastly argues that CMS failed to account for the effect of the Rule on innovation. CMS addressed this issue in its rulemaking. While CMS did not dispute that its interpretation of a line extension drug may result in a rebate amount that is greater than the standard rebate amount, it disagreed that the interpretation would "prevent a manufacturer from pursuing innovation." CMS stated that "[t]he fact that the innovation may lead to a higher rebate obligation for a drug that is a line extension is not the result of the innovation." 85 Fed. Reg. at 87,037. "Manufacturers will continue to have incentives to innovate based on multiple factors," such as "clinical significance of the drug, prescriber and patient demand, costs of research and development, and possible revenues generated." 85 Fed. Reg. at 87,036–37. Moreover, CMS specifically noted that "various FDA policies encourage innovation" and the Rule does not change "those FDA policies and incentives." *Id.* Indeed, the FDCA, administered by the FDA, governs the pharmaceutical drug approval process for both new and generic drugs. The Orphan Drug Act and Hatch–Waxman Amendments provide incentives, such as periods of market exclusivity for those pioneer manufacturers that invent new drugs. *See*, *e.g.*, *Otsuka Pharm. Co. v. Price*, 869 F.3d at 990; 21 U.S.C. § 360cc(a). CMS, an agency that administers the Medicaid Act, certainly would have a minimal role, in any, in influencing FDA's policies and incentives concerning pharmaceutical innovation.

Vanda insists that CMS was required to conduct a specific cost benefit analysis on the effect of the Rule on innovation. But none of the cases it cites supports Vanda's proposition. Additionally, even if such "cost benefit analysis" were required, CMS would not be able to conduct

such an analysis on "pharmaceutical innovation" because "[i]t is not privy to manufacturers' decision making, it does not have access to the projects manufacturers are planning, it does not set the drug prices for manufacturers." ECF 28 at 18. Vanda lastly warns about the dire consequences the Rule will have on pharmaceutical innovation. Congress, but not the Court, is better equipped to address Vanda's policy argument.

IV. Conclusion

For the reasons stated above, Plaintiff's motion for summary judgment (ECF 17) will be DENIED, and Defendant's cross-motion for summary judgment (ECF 26) will be GRANTED.

A separate Order will follow.

March 31, 2023
Date

/S/
Matthew J. Maddox
United States Magistrate Judge