No. 24-1187

In the Supreme Court of the United States

VANDA PHARMACEUTICALS INC.,

Petitioner,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION, et al.,

Respondents.

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

REPLY BRIEF FOR PETITIONER

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REPLY BRIEF FOR PETITIONER

Tradipitant is a drug with a demonstrated potential to help numerous patients suffering from gastroparesis, a severe and often debilitating stomach condition. It is precisely the sort of drug whose development Congress sought to incentivize and prioritize when it implemented the Fast Track program.

FDA nonetheless denied Vanda's request for fast-track status, insisting that non-statutory regulatory hurdles the agency itself had erected deprived tradipitant of the "potential" to help patients. In doing so, it departed from the statutory text, which focuses on the drug's potential *as a drug substance* to help patients, rather than on its potential to be approved under the sponsor's current development program. This is especially clear because FDA could exercise its discretion to lift the hold at any time.

In affirming the agency's interpretation, the D.C. Circuit reasoned that FDA's reading of the Fast Track statute was "reasonable" because the statute "leaves it for FDA to determine" whether a drug has the potential to address an unmet medical need. Pet. App. 15a-17a. Whatever popularity this deferential mode of judicial reasoning may have had decades ago, this Court has now made unmistakably clear that courts may not abdicate their primary responsibility as interpreters of statutory text. *Loper Bright Enters.* v. *Raimondo*, 603 U.S. 369, 400-401 (2024).

The Court should grant the petition to clarify both the statutory requirements for a program critical to drug manufacturers and patients and the proper role of courts under the Administrative Procedure Act after *Loper Bright*.

A. Tradipitant has the potential to help countless gastroparesis patients.

The Fast Track statute mandates that FDA provide the program's benefits to a "drug" that "is intended * * * for the treatment of a serious or life-threatening disease or condition, and * * * demonstrates the potential to address unmet medical needs for such a disease or condition." 21 U.S.C. § 356(b)(1). As FDA acknowledges (at 3), it has consistently recognized that gastroparesis is a serious condition with an unmet medical need. Rather than address tradipitant's *medical* potential, FDA sidestepped the issue by raising *regulatory* barriers it deemed dispositive. Neither FDA's unserious attempts to detract from tradipitant's proven potential to help patients nor its passing defense of the D.C. Circuit's deferential textual analysis comes remotely close to justifying its action below.

1. As Vanda explained (at 21-23), tradipitant has a well-demonstrated potential to address the unmet medical needs of gastroparesis patients. Vanda's four-week study showed a statistically significant reduction in gastroparesis patients' nausea—which FDA in another context recognized showed that tradipitant was a "*potential*" therapy "for the short-term relief of nausea in gastroparesis patients." C.A. J.A. 185-199, 657 (emphasis added). And tradipitant is *currently* being used to effectively treat nausea by dozens of patients as part of the Expanded Access program—it has received glowing reviews. Absent the agency's legal error (affirmed by the D.C. Circuit), it is apparent that tradipitant would warrant a fast-track designation.

FDA's response repeatedly misstates the record. It argues, for example (at 9), that the results of the

four-week study were not statistically significant. But the study's *primary* endpoint—reduction in nausea as measured by patients' nausea severity score—*was* statistically significant. C.A. J.A. 188. The study also showed that tradipitant had a statistically significant effect on patients' number of nausea-free days. *Ibid.*

And FDA's suggestion that Vanda's choice to allow severely ill patients enrolled in the trial to use rescue medications is a *methodological flaw* is little short of outrageous. FDA's own guidance recognizes that studies often *must* allow participants to take rescue medications and requires only that sponsors "clearly define how patients who take rescue medication will be considered in the final analysis." *Gastroparesis: Clinical Evaluation of Drugs for Treatment*, FDA 8 (Aug. 2019), perma.cc/T2WJ-YM5J. Vanda did just that, dividing the study population between those who did and did not use rescue medications during the trial. "The results were consistent across patients who used and did not use rescue medications," in that "[b]oth groups experienced significant improvements in average daily nausea and nausea-free days compared to placebo." C.A. J.A. 21.

Next, FDA attempts to downplay its own prior observation that there is a "potential therapeutic role for tradipitant" in the "treatment of gastroparesis." C.A. J.A. 657. While the agency requested additional information "before a Breakthrough Therapy Designation [was] possible," that does nothing to undermine the *potential* FDA recognized in tradipitant to treat gastroparesis patients' nausea. *Ibid.* Nor is it relevant that FDA couched its finding in a discussion of short-

term nausea treatments.[1] FDA has never identified any reason to suspect that tradipitant's efficacy in treating gastroparesis in the short term does not show at least the *potential* that it might treat it in the long term as well.

Finally, FDA brushes aside the real-life experience of the many patients who have successfully treated their gastroparesis with tradipitant through the Expanded Access program. It claims, in conclusory fashion, that Expanded Access and Fast Track are "governed by a different statutory standard" and are thus "wholly unrelated." BIO 9 (quoting Pet. App. 20a). But as we have already explained, for FDA to allow a patient to use tradipitant through Expanded Access, the agency necessarily "determine[d] that there is sufficient evidence of safety and effectiveness to support the use of the investigational drug" to treat these patients' medical needs, and that those needs were not adequately addressed by other therapies. 21 U.S.C. § 360bbb(b)(2). Beyond the appellate court's *ipse dixit*, FDA offers no clarity as to how it could possibly determine (repeatedly) that there is sufficient evidence to support the use of tradipitant to treat the

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[1] Elsewhere, FDA suggests that there are other therapies approved for the short-term treatment of gastroparesis. BIO at 7. But the agency overlooks that there are multiple distinct forms of gastroparesis, and there is *no* FDA-approved drug for idiopathic gastroparesis; metoclopramide is approved for diabetic gastroparesis only. C.A. J.A. 181. Tradipitant was studied for treatment of both conditions. C.A. J.A. 648. More, metoclopramide has a black-box warning disclosing severe and potentially irreversible side effects, and it can be used for only a limited time. This offers no solace to the many patients suffering from idiopathic gastroparesis who are unable to access tradipitant.

unmet medical needs of patients with gastroparesis in the Expanded Access program *and* that tradipitant lacks the potential to treat those same unmet medical needs for purposes of Fast Track.

2. Unable to defend FDA's fast-track denial on the merits, FDA makes a strained attempt to defend its atextual reading of the statute. It begins its opposition (at 7) with an enormous logical leap: because "potential" is prospective, a drug which faces a regulatory barrier to approval cannot have the potential to address patients' unmet medical needs. But that assumes away the entire interpretive dispute in this case; our *point* is that "potential" in the statute is about biological effects and not regulatory red tape. And in any event, just like the D.C. Circuit, FDA provides nothing to bridge that gap.

Instead, as we explained, a drug substance that is an effective treatment for a condition plainly has the "potential" to address unmet medical needs of suffering patients, regardless of regulatory hurdles to its approval. The Fast Track statute requires FDA to determine whether a "drug" has the potential to address a medical need. 21 U.S.C. § 356(b)(1). The FDCA defines "drug" to mean "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals." 21 U.S.C. § 321(g)(1). And the term "medical needs" describes a patient's individual treatment—and an area in which FDA is explicitly prohibited from regulating—as opposed to textual alternatives like "public health" that more naturally encompass the practical availability of a drug to the population. See Pet. at 18-20.

FDA's focus on a separate concept—a drug development program—is thus inconsistent with the text.

And it makes no sense. A drug can "address" a medical need by alleviating or curing a condition; it is incoherent to say that a drug development program "addresses" a patient's needs. Further, the benefits the Fast Track program provides—including a requirement that FDA "facilitate the development" of the drug—would be nullities if FDA could only award fast-track designations to drugs whose development programs FDA had already deemed sufficient. 21 U.S.C. § 356(b)(1).

FDA has no response to these arguments, or to the mountains of confirmatory legislative history. It offers instead (at 8) a single analogy of a "champion distance runner" banned for doping. But that analogy cannot withstand even the barest scrutiny.

Perhaps most obviously, the hypothetical is asking the wrong question. By focusing on whether the runner is permitted by the race organizers to compete in the official Boston Marathon, FDA again assumes its own conclusion: that "potential to address unmet medical needs" in the Fast Track statute is concerned with what regulators will allow, rather than what the drug substance (or the distance runner) is biologically capable of doing. The better hypothetical would be whether the banned runner, notwithstanding being banned, has the "potential" to run 26.2 miles faster than anyone else—and the answer to that question would be yes.[2]

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[2] Even setting aside that fundamental problem, the hypothetical fails on additional grounds as well. For one, FDA asks whether the runner has the potential to win "*this year's* Boston Marathon." BIO 8 (emphasis added). But the Fast Track statute contains no such temporal deadline, and any fluent speaker of

A better, real-world example is FDA's regulation of drugs derived from cannabis. FDA has approved several drugs containing cannabidiol and synthetic delta-9-tetrahydrocannabinol, both of which are active components of marijuana. The approved drugs were thus Schedule 1 drugs when they were approved. 21 U.S.C. § 802(16). As a result, those drugs "could not immediately be marketed in the United States" for "a few months to a couple years [after] their approval by FDA" until the Department of Justice rescheduled them. Dorothy C. Kafka, Cong. Rsch. Serv., LSB11227, *Legal Effect of Marijuana Rescheduling on FDA's Regulation of Cannabis* 3 (Sept. 16, 2024). FDA approved each drug knowing that a legal barrier prevented their widespread use in the United States. It is ridiculous to suggest that when FDA approved these drugs they lacked the potential to address the conditions for which they were approved.

While FDA may *wish* the statute pegged eligibility to approvability rather than the drug's substance, it is a "core administrative-law principle that an agency may not rewrite clear statutory terms to suit its own sense of how the statute should operate."

English would acknowledge that a champion runner subject to a temporary ban has the potential to win the Boston Marathon *in general*—once the ban no longer applies. Or consider a champion runner who was not eligible for the Boston Marathon because she had to run one additional qualifying race, or because she had yet to submit a required form. While the runner cannot, as things currently stand, compete in the race, it is obvious that she has the potential to win because the impediments to her doing so may be cured. The same is true of FDA's partial clinical hold—Vanda could submit the required study at any time (or FDA could relent in its demand for the study), rendering the hold an illusory barrier at most.

Utility Air Regul. Grp. v. *EPA*, 573 U.S. 302, 328 (2014). And this statute says no such thing.

3. The court of appeals affirmed FDA's reading of the statute only by applying an unacceptably deferential standard. That is, rather than determine the "single, best meaning" of the statute by exhausting the traditional tools of statutory interpretation (*Loper Bright*, 603 U.S. at 400), the court unduly deferred to FDA's approach.

In doing so, the D.C. Circuit resurrected the *Chevron* deference doctrine that this Court dispatched less than two years ago. It noted that the statutory language at issue was unclear. Pet. App. 15a. It described the best reading of the statute. Pet. App. 17a. ("The best reading of the statute indicates that, in enacting the fast track, Congress intended to benefit drugs that are not yet fully effective but that can demonstrate their potential effectiveness in addressing an unmet medical need in the future."). But rather than apply that straightforward reading to the facts at hand, the court instead deferred to FDA's interpretation as "reasonable" and "consistent with" the statutory scheme. *Ibid.*

FDA's attempt to recharacterize the opinion below is unpersuasive. Principally, it argues (at 11) that the court deferred not to FDA's interpretation of the Fast Track statute but to the agency's application of the text to the facts at hand. But just like FDA misreads Congress's language, it misreads the judicial language as well. The *entire* dispute between the parties below was whether FDA's reading—that ephemeral regulatory barriers to approval undo a drug's "potential" to treat unmet medical needs—was the proper interpretation of the statutory text. The court explained that

the statutory language required an assessment of whether a drug may "address[] an unmet medical need in the future." Pet. App. 17a. But it ended its analysis there, stating only that FDA's interpretation of the statutory requirement to also permit an inquiry into the drug's likelihood of *approval* was "reasonable." *Ibid.* This is a plain, straightforward abdication of judicial responsibility—the court allowed the agency to answer the statutory question rather than doing so on its own. *Loper Bright*, 603 U.S. at 401.[3]

B. This case is a rare, ideal vehicle to address an important, recurring question.

FDA offers no compelling reason why this Court should pass over this rare opportunity to stem the resurgence of *Chevron* deference and clarify the statutory requirements for a program critical to both patients and drug manufacturers.

1. The agency cannot deny what its own statistics show: Fast Track denials are frequent, but almost never judicially reviewed. FDA, *CDER Fast Track Designation Requests Received*, (Jan. 13, 2025), perma.cc/K2D5-673P (1,042 denials since 1998). As we explained, most pharmaceutical companies

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[3] To be sure, *Loper Bright* preserved the possibility that Congress might "authorize[]" an agency "to exercise a degree of discretion," such as by "'expressly delegat[ing]' to an agency the authority to give meaning to a particular statutory term," or by enacting standards such as "'appropriate' or 'reasonable'" that "leave[] agencies with flexibility." 603 U.S. at 394-395. But the Court certainly did not suggest that, in the absence of explicit term-defining authority, an agency's determinations about *what the law means*—as opposed to whether particular facts meet a statutory reasonableness standard—should receive deference from the courts.

hesitate to challenge FDA's decisions in court for a well-founded fear of retaliation. Pet. 35-36. The industry's reluctance will only deepen as lower courts fall back into familiar patterns of deference.

FDA is thus wrong to claim (at 12) that "this statutory-interpretation question * * * has arisen only once in 28 years." Rather, it occurs *often*, but evades judicial review. Pet. App. 14a. As the D.C. Circuit observed, there is a "reasonable expectation" that the issue will occur in future applications. *Ibid*. Indeed, FDA's approach to the Fast Track program guarantees that this issue will recur. The agency employs a checklist to evaluate applications which makes the existence of a clinical hold a categorical bar to Fast Track status. Pet. App. 8a; C.A. J.A. 329. The judgment below allows FDA to enshrine its atextual reading of the statute in agency policy, ensuring that future applications will be denied on the same basis as Vanda's. That is a compelling reason for this Court's intervention.

Review is especially critical here due to the importance of the Fast Track program to drug manufacturers and patients. Congress sought to incentivize the development of new therapies for patients with unmet medical needs by expediting FDA review and providing additional benefits. By improperly denying these benefits to drugs that can help (indeed, *have* helped) many patients, FDA undercuts this straightforward goal, resulting in a graveyard of unapproved or undeveloped therapies that could have benefited the American people.

2. The D.C. Circuit correctly rejected FDA's claim that the case is moot. Pet. App. 10a-14a. Vanda and FDA are, in fact, engaged in discussions about paths

forward for tradipitant; the parties recently agreed to an abeyance of *ongoing* legal proceedings about this new drug application, to allow "discussions" between FDA and Vanda to continue. See Revised Ltr. Re: CDER and Vanda's Joint Request, Docket No. FDA-2024-N-5933 (Oct. 20, 2025). A statutory obligation for FDA to facilitate the development program is a "concrete interest" that would benefit Vanda. Pet. App. 13a. In fact.

Additionally, this is an issue "capable of repetition yet evading review." Pet. App. 14a (quoting *Del Monte Fresh Produce Co.* v. *United States*, 570 F.3d 316, 322 (D.C. Cir. 2009)). As the D.C. Circuit observed, "the FDA has made it clear that it invites Vanda to submit a modified application for tradipitant indicated for short-term symptoms of gastroparesis." Pet. App. 14a. Thus, "there is 'a reasonable expectation that' any subsequent fast track applications will be subject to the same assessment process that Vanda alleges is improper here." *Id.* (quoting *Del Monte*, 570 F.3d at 322).

Meanwhile, Vanda continues to develop its innovative products. Vanda has submitted another NDA for tradipitant—to treat motion sickness. As Vanda develops novel therapies, it has every intention of submitting future Fast Track applications. FDA's misapplication of the statute—its use of an improper checklist—will continue to cause Vanda injury.

In short, because Vanda's new drug application for tradipitant will remain pending for the foreseeable future, Vanda has a continuing interest in adjudication of *this* Fast Track proceeding, as the court of appeals correctly held. Additionally, Vanda will continue to file similar applications, rendering this real dispute

between Vanda and FDA regarding the meaning of the Fast Tract statute one that has substantial prospective importance. FDA cannot shield this important statutory question—and the flawed statutory analysis employed below—from this Court's review.

CONCLUSION

The Court should grant the petition.

Respectfully submitted.

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