United States Court of Appeals

FOR THE DISTRICT OF COLUMBIA CIRCUIT

Argued September 25, 2024 Decided December 17, 2024

No. 23-5200

VANDA PHARMACEUTICALS, INC.,
APPELLANT

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION, ET AL.,
APPELLEES

Appeal from the United States District Court
for the District of Columbia
(No. 1:22-cv-01432)

Paul W. Hughes argued the cause for appellant. With him on the briefs were *Andrew Lyons-Berg* and *Tyler L. Bishop*.

Steven A. Myers, Attorney, U.S. Department of Justice, argued the cause for appellees. On the brief were *Brian M. Boynton*, Principal Deputy Assistant Attorney General, *Daniel Tenny* and *Anna M. Stapleton*, Attorneys, *Samuel Bagenstos*, General Counsel, U.S. Department of Health and Human Services, and *James Allred*, Associate Chief Counsel, U.S. Food and Drug Administration.

Before: KATSAS and CHILDS, *Circuit Judges*, and EDWARDS, *Senior Circuit Judge*.

Opinion of the Court filed by *Senior Circuit Judge* EDWARDS.

EDWARDS, *Senior Circuit Judge*: Companies seeking to market drugs in the United States must first obtain approval from the Food and Drug Administration ("FDA"). 21 U.S.C. § 355(a). Seeking to expedite this process, Congress enacted a "fast track" approval program, pursuant to which the FDA shall "facilitate the development and expedite the review" of a new drug if it "demonstrates the potential to address unmet medical needs" for a serious disease or condition. 21 U.S.C. § 356(b)(1). The dispute in this case concerns a fast track request filed by Vanda Pharmaceuticals, Inc. ("Vanda") with the FDA for tradipitant, an investigational new drug product that Vanda is developing for the treatment of gastroparesis. Vanda claims that the FDA's denial of fast track designation for tradipitant was contrary to law, and arbitrary and capricious agency action.

Before Vanda's fast track request was filed, the FDA had placed its drug on a partial clinical hold, as authorized by 21 U.S.C. § 355(i)(3). The clinical hold prevents any long-term clinical studies on Vanda's drug until long-term animal studies have been completed to assess its toxicological effects. When the FDA later assessed Vanda's eligibility for fast track, the clinical hold was a significant factor that led the agency to deny Vanda's request. The FDA essentially determined that, without long-term studies, Vanda could not "demonstrate" that its drug had the "potential to address" the unmet need for long-term treatment of gastroparesis.

Vanda challenges the FDA's denial as arbitrary, capricious, and contrary to law under the Administrative Procedure Act ("APA"), 5 U.S.C. § 706(2)(A). It contends that the FDA erred in considering the clinical hold as a factor,

improperly defined the "unmet medical need" at issue to constitute long-term treatment only, and adopted a view of the fast track program that was at odds with agency practice.

The District Court granted summary judgment for the FDA and Vanda sought review in this court. While this appeal was pending, Vanda also filed a complete New Drug Application ("NDA") for its drug, which the FDA has since denied in its current form. This complete filing, the FDA argues, has mooted the question presented here. We disagree, and affirm the District Court's decision on the merits. The FDA properly considered the drug's development plan in assessing whether it qualified for fast track, and its denial of Vanda's fast track application was neither contrary to law nor arbitrary and capricious.

I. BACKGROUND

A. Statutory and Regulatory Framework

Before a new drug may be marketed in the United States, the FDA must first confirm that it is safe and effective. Food, Drug and Cosmetic Act ("FDCA"), 21 U.S.C. § 355(d). The FDA process generally takes approximately ten months. Manufacturers seeking to better study their drugs before filing a marketing application may submit an Investigational New Drug Application ("IND") to the FDA. *Id.* § 355(i)(1), 21 C.F.R. § 312.20(a). The IND allows manufacturers to run clinical trials before obtaining marketing approval. However, if the FDA finds that the drug in question "represents an unreasonable risk to the safety" of test subjects, it may impose a clinical hold on such studies. 21 U.S.C. § 355(i)(3)(B). A clinical hold halts any further studies or trials until the manufacturer cures the issues that give the FDA pause.

Aiming to "hasten research of the safety and effectiveness of drugs" in some cases, Congress has enacted several programs to expedite the FDA's review process. *Abigail All. for Better Access to Developmental Drugs v. von Eschenbach*, 495 F.3d 695, 699, n.4 (D.C. Cir. 2007). One such program, for instance, designates a drug as a "breakthrough therapy" if "preliminary clinical evidence" indicates that the drug offers a "substantial improvement over existing therapies." 21 U.S.C. § 356(a)(1). Another expedited review pathway is "accelerated approval," which may be granted if the FDA determines that the drug in question "has an effect" that is "reasonably likely to predict clinical benefit" for a condition, considering its "severity, rarity, or prevalence" and the "lack of alternative treatments." *Id.* § 356(c)(1).

At issue here is the specific expedited program known as "fast track." Enacted as part of the FDA Modernization Act of 1997, the fast track statute provides that the FDA "shall take such actions as are appropriate to expedite the development and review" of a drug that is intended "for the treatment of a serious or life-threatening disease or condition" if the drug in question "demonstrates the potential to address unmet medical needs for such a disease or condition." *Id.* § 356(b)(1), (b)(3).

A fast track designation offers two main benefits to a drug manufacturer. First, the FDA will "facilitate the development" of the drug, usually by providing feedback in ongoing discussions with the manufacturer. *Id.* § 356(b)(1); FDA, *Guidance for Industry: Expedited Programs for Serious Conditions – Drugs and Biologics*, Joint Appendix ("J.A.") 672. Second, fast track drugs are reviewed on an expedited schedule, and are considered for expedited review programs. These include the accelerated approval program under section 356(c) and "rolling review," in which the FDA provides feedback to the manufacturer on individual portions of the

application so that the developer may make any revisions before filing a complete NDA. 21 U.S.C. § 356(d)(1).

Applicants may request a fast track designation "concurrently with, or at any time after" their IND submission. *Id.* § 356(b)(2). In reviewing requests for fast track, the FDA requires that manufacturers list their drug's proposed indication in the application. Where a drug may have more than one indication, applicants may file multiple fast track requests or list multiple indications in the same application.

B. Factual Background

In 2016, Vanda submitted an IND to begin studying its drug tradipitant for the treatment of gastroparesis, a chronic stomach condition with persistent symptoms that include abdominal pain, vomiting, and nausea. Vanda reported that preliminary studies on gastroparesis patients in a four-week drug trial showed that tradipitant had a statistically significant effect on one of the "core" symptoms of gastroparesis, nausea.

There are two kinds of gastroparesis: idiopathic and diabetic. The FDA currently recognizes one approved drug for diabetic gastroparesis, which is only indicated for short-term use of up to three months due to risks of serious side effects after 12 months of use. There are no FDA-approved drugs specifically for idiopathic gastroparesis, although the treatment of its symptoms – including nausea – is the same as for diabetic gastroparesis.

Vanda's relevant discussions with the FDA regarding tradipitant began in April 2018, when it submitted a proposal to extend its four-week clinical trial of the drug by 12 months. The FDA denied this proposal, requiring a nine-month animal study to assess the drug's long-term toxicity before Vanda

could proceed with long-term studies in humans. Vanda refused to conduct such studies, citing its ethical opposition to nonrodent testing that requires sacrificing the animal. As a result of this refusal, the FDA imposed a partial clinical hold, as authorized by 21 U.S.C. § 355(i)(3), which prevents further long-term clinical studies until Vanda conducts the required animal studies. While the hold is in place, Vanda can still conduct short-term clinical studies. In a separate litigation, Vanda sought judicial review of the clinical hold and the District Court upheld the FDA's order. *Vanda Pharm., Inc. v. FDA* ("*Vanda I*"), 436 F. Supp. 3d 256 (D.D.C. 2020). Vanda did not appeal this decision.

In March 2019, Vanda requested that tradipitant be designated a "breakthrough therapy" for the treatment of gastroparesis under 21 U.S.C. § 356(a). Pointing to issues with the study's conclusions and its findings of the drug's effectiveness on nausea symptoms, the FDA denied this request. The FDA also advised Vanda that it was "considering an indication for the short-term relief of nausea in gastroparesis" and encouraged Vanda to "further evaluate tradipitant for this use" in future submissions. Letter from FDA Director Julie Beitz to Vanda Denying Appeal of Denial of Breakthrough Therapy Designation for Tradipitant (Feb. 28, 2020) [*hereinafter* FDA Letter Affirming Breakthrough Therapy Designation Denial], J.A. 657.

Finally, in 2021, Vanda filed the fast track application that is the subject of this litigation. Rather than taking the FDA's recommendation to tailor its application to short-term relief, Vanda once again framed tradipitant's indication as for the symptoms of gastroparesis broadly. As with its previous applications, Vanda's fast track request described the symptoms of gastroparesis as "chronic" and "persistent," with most patients "requir[ing] long-term medications." Vanda

Pharma., Inc., Request for Fast Track Designation 8-11 (Sep. 28, 2021), J.A. 177-80.

The FDA denied Vanda's fast track request. While it conceded that gastroparesis is a serious condition with an unmet medical need, the agency found that the partial clinical hold prevented Vanda from demonstrating that its drug could address that need. This was because, being unable to conduct long-term studies, Vanda could not obtain the data necessary to demonstrate the product's potential for the indication as described in its application – *i.e.*, to treat the symptoms of gastroparesis, which are chronic, rather than to provide short-term symptomatic relief.

In a contemporaneous internal memorandum, the FDA elaborated that the unmet medical need tradipitant purported to address was the long-term treatment of nausea symptoms, but that no data on the drug's effectiveness for this indication could be generated while the clinical hold was in place. The FDA further observed that the approach to treating nausea in patients was the same whether the gastroparesis was diabetic or idiopathic. The FDA also noted issues with Vanda's study's methodology, including the use of rescue medication, which the FDA was concerned may have tainted the results of Vanda's study. These internal notes, although not originally disclosed to Vanda, mirror feedback that Vanda had previously received from the FDA in connection with its breakthrough designation application.

The FDA's memo also included an internal checklist that the FDA uses to assess fast track applications. The checklist contains six main items, including whether the condition is serious/life-threatening, and whether the product's development program was designed to demonstrate an effect on a serious aspect of the condition. For these two items – items

1 and 2 – the FDA marked "yes" when assessing Vanda's fast-track application. But it marked "no" as to items 3 and 4, which ask if the product development plan addresses an unmet medical need and if the product shows potential to address an unmet medical need. Also relevant is item 5, which asks whether the data supporting the request comes from trials that are on clinical hold. Here, the FDA marked "yes." The checklist then recommends that, for fast track approval, items 1 through 4 must be answered "yes," and that, if item 5 is marked "yes," – *i.e.*, if there is a clinical hold in place – the fast track application may not be granted.

In the face of the fast track denial and of the partial clinical hold, Vanda could then pursue one of two courses of action. First, it could file a new fast track application, tailored to the short-term treatment of gastroparesis symptoms, as the FDA suggested it do. Alternatively, it could conduct the required animal studies to lift the clinical hold and proceed with long-term studies to treat gastroparesis broadly. Vanda chose to pursue neither of these options, which have remained open in the course of this litigation. Instead, it filed suit in federal court challenging the fast track denial as arbitrary and capricious under the APA. While the District Court's decision on cross-motions for summary judgment was pending, Vanda then submitted a complete NDA, requesting marketing approval of its drug – once again, indicated broadly to treat gastroparesis symptoms. The District Court granted summary judgment in favor of the FDA. This appeal followed.

After this appeal was filed, the FDA reviewed Vanda's NDA and issued a Complete Response Letter denying the application in its current form, finding that Vanda does not provide substantial evidence of effectiveness for tradipitant for the treatment of either symptoms of gastroparesis more broadly or nausea specifically.

II. ANALYSIS

A. Standard of Review

This Court reviews appeals from summary judgments *de novo*, applying the standards set forth in Federal Rule of Civil Procedure 56(a). *See, e.g.*, *Celotex Corp v. Catrett*, 477 U.S. 317, 322 (1986). Under Rule 56(a), summary judgment is warranted if the movant shows that "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law."

When reviewing agency decisions under the APA, we set aside agency actions if we determine that they are "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). An agency "acts arbitrarily or capriciously if it 'has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise.'" *Am. Wildlands v. Kempthorne*, 530 F.3d 991, 997-98 (D.C. Cir. 2008) (quoting *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983)).

Where the question is whether the agency action was consistent with statutory authorization, our task is to determine whether the agency acted consistently with the "best reading" of the statute. *Loper Bright Enterprises v. Raimondo*, 144 S. Ct. 2244, 2263 (2024). This judicial inquiry includes a determination as to whether the statute in question "delegates discretionary authority" to the agency and whether the agency "engaged in reasoned decisionmaking within [the] boundaries"

of that statutory delegation. *Id.* (internal quotation marks and citations omitted).

B. Finality and Mootness

As a threshold matter, it is not clear that the denial of fast track review is a final action that is subject to judicial review. *See Bennett v. Spear*, 520 U.S. 154, 177-78 (1997). This is because normally "[a] preliminary, procedural, or intermediate agency action or ruling" is only "subject to review on the review of the final agency action." *Yaman v. U.S. Dep't of State*, 634 F.3d 610, 613 (D.C. Cir. 2011) (*per curiam*) (quoting 5 U.S.C. § 704).

This final order rule codifies the understanding that "[p]remature review squanders judicial resources," and that litigants are generally "best served by a system which prohibits piecemeal appellate consideration of rulings that may fade into insignificance by the time proceedings conclude." *CSX Transp., Inc. v. Surface Transp. Bd.*, 774 F.3d 25, 31 (D.C. Cir. 2014) (internal quotation marks and citations omitted). Thus, we normally "reserv[e] judicial review until the end of an adjudication," when a judgment has been rendered on the merits of the matter before the agency – in this case, until the final completed NDA is ultimately denied. *Id.*; *see also Holistic Candlers & Consumers Ass'n v. FDA*, 664 F.3d 940, 943 (D.C. Cir. 2012) (finding that FDA warning letters are not reviewable final agency actions because they "neither mark the consummation of the agency's decisionmaking process nor determine the appellants' legal rights or obligations").

Neither party contends that the FDA's Complete Response Letter denying the NDA in its current form is a final agency action, as it "simply afford[s] [Vanda] the opportunity to provide additional information before the agency makes a

final decision on the application." *Nostrum Pharms., LLC v. FDA*, 35 F.4th 820, 825 (D.C. Cir. 2022) (holding that a "complete response letter is an interim step in the FDA's consideration of an application" and, therefore, not a final agency action under 21 U.S.C. § 355(h)). Indeed, the Complete Response Letter is not at issue in this case.

It is thus unclear under applicable law whether the FDA's denial of fast track review of Vanda's application, on its own, is a final order. We leave this question for another day, however, because the FDA does not claim the disputed action taken on Vanda's fast track request was not a final action subject to judicial review. As finality is not jurisdictional under the APA, we therefore need not decide this matter. *See Marcum v. Salazar*, 694 F.3d 123, 128 (D.C. Cir. 2012). Rather than challenge finality, the FDA alleges a different justiciability bar, contending that the fast track issue should be dismissed as moot. We disagree.

We are "obliged to address the issue" of mootness because it "goes to the jurisdiction of this court." *Row 1 Inc. v. Becerra*, 92 F.4th 1138, 1143 (D.C. Cir. 2024) (internal quotation marks and citation omitted). A claim is moot when "the issues presented are no longer 'live' or the parties lack a legally cognizable interest in the outcome." *Already, LLC v. Nike, Inc.*, 568 U.S. 85, 91 (2013) (quoting *Murphy v. Hunt*, 455 U.S. 478, 481 (1982) (*per curiam*)). Intervening events may moot a claim if they "make it impossible to grant the prevailing party effective relief." *Lemon v. Geren*, 514 F.3d 1312, 1315 (D.C. Cir. 2008) (internal quotation marks and citation omitted). While the party invoking mootness "bears the initial burden of proving that no live controversy exists," *N. Am. Butterfly Ass'n v. Wolf*, 977 F.3d 1244, 1258 (D.C. Cir. 2020) (internal quotation marks and citation omitted), this court still has the "independent obligation to ensure that appeals before us are not

moot." *Planned Parenthood of Wis., Inc. v. Azar*, 942 F.3d 512, 516 (D.C. Cir. 2019) (internal quotation marks and citation omitted).

The FDA contends that the denial of fast track review is not a live issue at this juncture because any benefits of fast track are inapplicable once the complete NDA has been filed. But fast track is not an "all or nothing" package: that Vanda cannot at this stage benefit from all of the features of the fast track program, such as rolling review, does not mean it has no concrete interest in the program. Because Vanda can still benefit from other advantages the program confers, including expedited review and facilitation opportunities, it retains a "legally cognizable interest" in the resolution of the question before us here. *Already*, 568 U.S. at 91.

First, now that the FDA has denied Vanda's NDA in its current form, Vanda may continue to discuss how to move forward with its application, and will benefit from facilitation of the drug's development in these negotiations. We see no reason why a fast track designation would confer no relief in this ongoing process, and why it would therefore be "impossible for a court to grant any effectual relief" to Vanda if we determine that it should prevail on the merits. *Knox v. Serv. Emps. Int'l Union, Loc. 1000*, 567 U.S. 298, 307 (2012) (internal quotation marks and citation omitted). Even if the benefits of such facilitation discussions are marginal in the face of the substantial feedback Vanda has already received, this concrete interest, "however small," means that the case is not moot. *Id.*

Second, while the application is in continued revision, fast track status would still confer the concrete benefit of expedited "review of the application" under section 356(b). Should Vanda prevail on the merits, it would thus obtain the

"opportunity to pursue a benefit" of expedited review of its application, which is a "constitutionally cognizable" interest. *CC Distribs., Inc. v. United States*, 883 F.2d 146, 150 (D.C. Cir. 1989).

The FDA argues that completed NDAs are only reviewable in an expedited fashion under "priority review," a separate review program which assesses whether the drug in question would provide a significant improvement in safety and effectiveness. It points to the fact that in filing its NDA, Vanda concurrently requested priority review of its application. But the fact that a complete NDA may benefit from priority review does not necessarily mean that it cannot also qualify for fast track. In fact, fast track applications may be filed "any time after" the IND is submitted. 21 U.S.C. § 356(b)(2). Nor are these two expedited review pathways interchangeable because, as the FDA acknowledges, an application meeting the criteria for fast track would not necessarily qualify for priority review. Thus, Vanda could still receive the benefit of expedited review "of the application" if it meets the fast track statutory criteria, which are different from those for priority review.

Finally, even if the fast track status were a moot issue, the facts here involve an agency action "capable of repetition yet evading review." *Del Monte Fresh Produce Co. v. United States*, 570 F.3d 316, 322 (D.C. Cir. 2009). This exception to the mootness doctrine applies "where (1) the challenged action is in its duration too short to be fully litigated prior to cessation or expiration, and (2) there is a reasonable expectation that the same complaining party will be subject to the same action again." *Kingdomware Techs., Inc. v. United States*, 579 U.S. 162, 170 (2016) (cleaned up).

Because fast track applications must be reviewed within 60 days, 21 U.S.C. § 356(b)(3), the challenged action here is

"too short to be fully litigated prior to its cessation or expiration." *Del Monte*, 570 F.3d at 322 (noting that "agency actions of less than two years' duration cannot be 'fully litigated' prior to cessation or expiration"). And because the FDA has made it clear that it invites Vanda to submit a modified application for tradipitant indicated for short-term symptoms of gastroparesis, 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.*

We therefore proceed to the merits of Vanda's claim.

C. *The FDA's Denial of Vanda's Fast Track Application Was Not Contrary to Law*

Vanda first argues that the text of section 356(b) prohibits the FDA from considering a clinical hold or other elements of the drug's development program when assessing a fast track application. We disagree.

There are some provisions in the FDCA that are relatively clear in indicating how the FDA should designate certain products. *See, e.g.*, *Genus Med. Techs. LLC v. FDA*, 994 F.3d 631, 633 (D.C. Cir. 2021) (interpreting FDCA provisions for designation of products as "drugs" or "devices" where the statute defined each term and rejecting the FDA's interpretation as inconsistent with the relevant statutory definitions). The same is not true with respect to the fast track provision in the FDCA. Rather, the statute leaves it for the FDA to determine whether a drug "demonstrates the potential to address unmet medical needs," 21 U.S.C. § 356(b)(1), (b)(3), and it does not define these terms. The statute merely encourages the FDA to "utilize innovative and flexible

approaches to the assessment of products" that address "unmet medical needs." *Id.* § 356(e)(1).

Vanda contends that the FDA could not consider the clinical hold because the statute's text allows the FDA to only consider the "drug," not the drug's development program. In other words, Vanda argues that because the statutory language requires the FDA to assess whether *the drug* demonstrates the potential to address unmet medical needs, the FDA impermissibly deviated from the statute when it considered the drug's *development program*, including whether a clinical hold was in place. This is an untenable distinction.

The statute places the burden on an applicant to "demonstrate" that its drug meets the fast track criteria. To assess whether this standard is met, the FDA obviously must consider how the application puts forth the drug's capacity to address the indicated need. In doing so, the FDA may consider past studies that have been conducted and how future studies may further offer evidence of the drug's efficacy. *See Prohibition Juice Co. v. FDA*, 45 F.4th 8, 26 (D.C. Cir. 2022) (explaining that the FDA shall deny an application where the statute "requires that applicants make a certain showing before their products can be approved" and the "applicant[s] fail[] to make that showing"). Vanda points to no statutory language to the contrary. Moreover, the fast track provision requires the FDA to assess not only whether the drug currently addresses unmet needs, but whether it has the "potential" to address them. This language mandates an inherently prospective analysis. *See Potential*, OXFORD ENGLISH DICTIONARY (2d ed. 1989). The drug's development plan, including what past and future studies may demonstrate about the potential of the drug, are plainly relevant and permissible considerations.

Vanda's self-serving interpretation of the statute is both under- and overinclusive. It would preclude the FDA from considering a drug's development plan at all, even where it might be lenient to an applicant whose drug has yet to show results and who can only demonstrate its potential through a development plan that may in the future prove the drug's effectiveness. Simultaneously, Vanda would require that the FDA grant fast track to all applications that show that the drug might in the future serve an unmet need, even if current studies do not show that it is effective and future studies cannot be conducted. Such a construction of the statute would render superfluous the FDA's role in determining whether a drug "demonstrates" the potential defined by the statute, as it would make virtually all drugs intended for treating the qualifying conditions eligible for fast track. *See Donnelly v. FAA*, 411 F.3d 267, 271 (D.C. Cir. 2005) ("We must strive to interpret a statute to give meaning to every clause and word, and certainly not to treat an entire subsection as mere surplusage.").

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. Assessing the drug's development plan, including whether future studies may be conducted to demonstrate its potential or cure current data issues, is perfectly consistent with that goal. By considering all available evidence, the FDA thus lives up to the statutory mandate that it "utilize innovative and flexible approaches" to determine whether to grant fast track status, especially where current data on the drug's effectiveness may be scarce at the time the FDA is evaluating it for fast track. 21 U.S.C. § 356(e)(1).

The FDA previously informed Vanda of numerous concerns it had about its tradipitant study. In the face of such

issues with existing data, the agency's consideration of whether future studies might cure those problems is entirely consistent with the statute's mandate. It was equally reasonable for the FDA to conclude that Vanda's decision not to conduct additional studies required to lift the partial clinical hold meant that Vanda would not cure those issues and, thus, could not demonstrate tradipitant's potential to address the unmet need that Vanda's application identified.

D. The FDA Did Not Act Arbitrarily and Capriciously in Denying Vanda's Fast Track Application

On the record before us, we also conclude that the FDA did not act arbitrarily or capriciously in assessing Vanda's fast track application.

First, it was permissible for the FDA to assess tradipitant as indicated for long-term symptoms of gastroparesis. The record – including Vanda's own filings with the FDA – makes clear that gastroparesis is a chronic disease. Indeed, the fact that Vanda had previously sought to extend its clinical trials to 12 months indicates that it was interested in tradipitant's long-term effects. And, even after the FDA advised Vanda that it should tailor its future submissions more narrowly to short-term symptoms, Vanda did not do so, continuing to list tradipitant's indication as for the treatment of symptoms of gastroparesis broadly. The fact that Vanda chose not to follow that recommendation does not place the burden on the FDA to divine a more specific indication for the drug than what Vanda described in its application.

Moreover, as Vanda itself acknowledged in its application, there is already a FDA-approved short-term treatment for gastroparesis. In light of this alternative treatment and of Vanda's own description of the condition it set out to treat, the

FDA was reasonable in defining the unmet medical need as the need for long-term treatment of gastroparesis symptoms. And, because the clinical hold precludes Vanda from demonstrating that its drug will be an improvement on the current treatment's toxic long-term side effects, it was also reasonable for the FDA to conclude that tradipitant could not demonstrate that it had the potential to meet that need.

Second, it was also reasonable for the FDA not to address tradipitant's indication to treat *idiopathic* gastroparesis separately, because the version of the disease is irrelevant to the drug's effectiveness to treat chronic nausea symptoms. Vanda contends that, because idiopathic gastroparesis in particular has no FDA-approved treatment, the FDA should have granted fast track to tradipitant for that narrower indication. But the lack of any approved idiopathic gastroparesis treatment does not mean that tradipitant necessarily meets that need. In fact, the record shows that tradipitant's only statistically significant effects are on the symptom of nausea, which manifests the same way in both idiopathic and diabetic gastroparesis. The FDA's concerns with Vanda's nausea findings and with the clinical hold's foreclosure of long-term studies apply just as compellingly to an indication for idiopathic gastroparesis as they do for gastroparesis generally.

Finally, Vanda argues that the FDA had already previously indicated that tradipitant had "potential," and had already approved it for treatment in some circumstances, so the fast track denial was an arbitrary contradiction of the agency's prior positions. This claim is without merit. An agency acts unreasonably when it deviates from prior positions "in similar situations," which is plainly not the case here. *Gen. Motors Corp. v. Nat'l Highway Traffic Safety Admin.*, 898 F.2d 165, 174 (D.C. Cir. 1990).

Vanda first points to a letter in which an FDA director, while affirming the FDA's denial of breakthrough therapy designation under the separate standard governed by section 356(a), states that she saw "a potential therapeutic role for tradipitant, particularly for the short-term relief of nausea in gastroparesis patients." FDA Letter Affirming Breakthrough Therapy Designation Denial, J.A. 657. But this non-binding statement assessed tradipitant's merits under the separate standard of section 356(a), and thus cannot indicate a shift in agency position with regards to whether tradipitant met the different criteria for fast track under section 356(b). *See Gen. Motors Corp.*, 898 F.2d at 174; *Muwekma Ohlone Tribe v. Salazar*, 708 F.3d 209, 216 (D.C. Cir. 2013) (finding no inconsistency where the agency's positions did not involve treating "similar situations differently").

In any event, the FDA's denial of both requests reflects a consistent position, as the agency asserted many of the same issues with the drug's studies in both decisions. Immediately after the language Vanda quotes, the FDA director observed that "additional data would be needed" to support a breakthrough therapy designation. FDA Letter Affirming Breakthrough Therapy Designation Denial, J.A. 657. The director also added that Vanda's application was for a broader indication than its data supported, as it was "for 'the treatment of gastroparesis', not for the treatment of a single symptom associated with gastroparesis." *Id.* Instead, the agency advised that Vanda "should not submit a request for Breakthrough Therapy Designation to treat 'gastroparesis' based on a treatment effect for nausea alone." *Id.* The FDA's denial of Vanda's fast track application is therefore consistent with its prior feedback to Vanda, including that its current data did not demonstrate the potential for tradipitant to treat gastroparesis symptoms generally.

Vanda's second contention of a prior inconsistent agency position is equally unpersuasive. Vanda refers to the FDA's prior approval of expanded access for tradipitant, which is not only governed by a different statutory standard under 21 U.S.C. § 360bbb(b)(2), but is also wholly unrelated to expedited approval. The expanded access program allows physicians, subject to certain conditions, to request manufacturers to provide an unapproved, investigational drug for the treatment of specific patients, whom the physician in question will monitor. *Id.* § 360bbb(b). Unlike breakthrough therapy, accelerated approval, and fast track, expanded access does not expedite a drug's approval process. It merely authorizes its use for certain patients in certain conditions if "the Secretary determines that there is sufficient evidence of safety and effectiveness to support the use of the investigational drug" in the unique case of each petitioning patient. *Id.* § 360bbb(b)(2).

Vanda argues that because the FDA had already granted expanded access for tradipitant to eight individuals, some of whom have used the drug for over a year, tradipitant's "potential" under section 356(b) is met, and the FDA's fast track denial was therefore inconsistent with the expanded access grant. But authorization for expanded access takes no position on the drug's marketing approval, likelihood of success, or potential to treat patients on a broader scale. There is no inconsistency between the FDA's grant of expanded access and its denial of fast track where these two programs operate under different statutory standards and objectives.

Finally, Vanda's ethical objections to the required animal studies to lift the clinical hold, principled though they may be, are beside the point. Having fully litigated the propriety of the clinical hold in *Vanda I*, Vanda is estopped from raising any new challenges to the hold that it could have raised earlier. *See Ashbourne v. Hansberry*, 894 F.3d 298, 302 (D.C. Cir. 2018).

Vanda attempts to circumvent res judicata by raising the novel argument that the FDA Modernization Act 2.0, Pub. L. No. 117-328, enacted after *Vanda I*, now renders the clinical hold unreasonable. But we do not reach this claim because Vanda raises it for the first time on appeal, even though the relevant statute was enacted before the District Court reached its decision. *See Zevallos v. Obama*, 793 F.3d 106, 114 (D.C. Cir. 2015). Vanda is welcome to raise this argument before the FDA as it continues to discuss tradipitant's approval, as the FDA is better positioned to assess the reasonableness of scientific methodology than this court. *See Smith v. Berryhill*, 587 U.S. 471, 488 (2019) ("[A] federal court generally goes astray if it decides a question that has been delegated to an agency if that agency has not first had a chance to address the question.").

In light of the evidence before it, the FDA reasonably interpreted Vanda's fast track application as targeting the chronic symptoms of gastroparesis, which necessarily requires that tradipitant meet the unmet need for long-term treatment. The FDA's focus on the drug's effects on chronic symptoms is wholly consistent with the record and demonstrates a "rational connection between the facts found and the choice made." *State Farm*, 463 U.S. at 43 (internal quotation marks and citation omitted); *see also Growth Energy v. EPA*, 5 F.4th 1, 16 (D.C. Cir. 2021) (*per curiam*) ("[B]ecause the agency examined the relevant data and articulated a satisfactory explanation for its action, we uphold its decision." (internal quotation marks and citation omitted)). We therefore find that the FDA's denial of Vanda's fast track application was neither arbitrary nor capricious.

III. CONCLUSION

For the reasons set forth above, we affirm the District Court's grant of summary judgment to the FDA. Vanda remains free to continue its negotiations with the agency, including to file an amended application pursuing a short-term indication for its drug, or to proceed to lift the partial clinical hold.

So ordered.