IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

VANDA PHARMACEUTICALS INC.,
2200 Pennsylvania Avenue NW
Suite 300E
Washington, DC 20037,

Plaintiff,

v.

FOOD AND DRUG ADMINISTRATION,
10903 New Hampshire Avenue
Silver Spring, MD 20993,

ROBERT M. CALIFF, M.D.,
in his official capacity as Commissioner of Food and Drugs,
10903 New Hampshire Avenue
Silver Spring, MD 20993,

UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES
200 Independence Avenue SW
Washington, DC 20201,

and

XAVIER BECERRA, in his official capacity as Secretary of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201,

Defendants.

Civ. No. 24-cv-351

COMPLAINT

Plaintiff Vanda Pharmaceuticals Inc. (Vanda) brings this complaint against the Food and Drug Administration (FDA), the Department of Health and Human Services, Robert M. Califf, and Xavier Becerra, and alleges as follows:

INTRODUCTION

1. Quite recently, this Court reiterated to FDA how the statutory deadlines for resolving new drug applications operate. *See Vanda Pharms. Inc. v. FDA*, 2024 WL 307387 (D.D.C. Jan. 26, 2024). Despite that judicial reiteration, FDA continues to flout statutory deadlines—this time, with Vanda's supplemental new drug application seeking approval to market Hetlioz® tasimelteon to treat insomnia characterized by difficulties with sleep initiation. As for this program, on Sunday, February 4, 2024, FDA sent Vanda a "Deficiencies Preclude Discussion" letter,[1] clearly signaling that FDA does not intend to approve Vanda's pending sNDA. But rather than adhere to governing statute—which requires FDA to either approve the sNDA or provide Vanda a notice of an opportunity for a hearing so as to proceed with the regulatory process—FDA has insulated itself from judicial review via processes that create extra-statutory delay. Given FDA's demonstrated pattern of delay, Vanda asks the Court to compel FDA to act on its application and to invalidate FDA's regulations that effect an end-run around the timetable Congress mandated.

2. The FDA has a statutory obligation to act on a drug manufacturer's new drug application (NDA) or supplemental new drug application (sNDA) within a set time frame. Specifically, FDA has a non-discretionary duty under the Federal Food, Drug, and Cosmetic Act (FDCA) to either approve an NDA or publish notice of an opportunity for a hearing in the Federal Register within 180 days of the filing of the application. 21 U.S.C. § 355(c)(1); 21 C.F.R. § 314.100(a).

3. Despite this clear statutory text, FDA has sought to substantially expand the time it has to respond, both by regulation and by a practice of flouting the statutory deadline. To start,

[1] FDA no doubt sent this letter on a Sunday *because* it was the *regulatory* deadline for sending it. FDA treats its regulations as binding law—rather than the federal statute.

FDA regulations artificially extend the review period by giving itself an additional 60 days at the beginning of the process to determine whether an application can even be "filed." Then, FDA purports to suspend the 180-day deadline during any period after the agency sends the applicant a "complete response letter" identifying problems with the NDA, and before the applicant takes one of a list of specified actions. This effectively turns the FDCA's mandatory deadline into a nullity.

4. Neither of these regulations is lawful. Indeed, this Court has already determined that "the FDA's regulations conflict with the tighter statutory requirements." *Vanda Pharms. Inc. v. FDA*, 2024 WL 307387 (D.D.C. Jan. 26, 2024). It is a core principle of administrative law that an agency may not "rewrite clear statutory terms to suit its own sense of how the statute should operate." *Util. Air Reg. Grp. v. EPA*, 573 U.S. 302, 328 (2014). Statutorily mandated deadlines are no exception—an agency has no authority to "grant itself unlimited time to act" when Congress sets a mandatory deadline for agency action. *Allegheny Def. Project v. FERC*, 964 F.3d 1, 17 (D.C. Cir. 2020) (en banc). Yet, that is exactly what FDA has done here. And to make matters worse, FDA's adoption of the regulations at issue is inconsistent with the Constitution's Appointments Clause several times over.

5. Moreover, FDA's complete response regulations effectively enable the agency to escape judicial review altogether by allowing it to avoid *ever* giving a drug applicant a final denial of an NDA. *See Nostrum Pharms., LLC v. United States Food & Drug Admin*., 35 F.4th 820, 826 (D.C. Cir. 2022) (holding that a complete response letter is not a final agency action entitled to judicial review). Given that most drug sponsors that receive a complete response letter never move past that stage—by seeking a notice of an opportunity for a hearing, proceeding through FDA's time-unlimited summary-judgment process, and then through a hearing process—all to obtain the final order rejecting their applications, FDA has effectively insulated itself from judicial review of its decisionmaking by interposing unlawful protracted processes. *See Environmental Defense Fund, Inc. v. Ruckelshaus*, 439 F.2d 584, 593 (D.C. Cir. 1971) (if court has jurisdiction to review

agency denial of a petition, agency cannot escape review by "delaying [its] determination indefinitely"); *Cobell v. Norton*, 240 F.3d 1081, 1095 (D.C. Cir. 2001) (noting that, without the court's ability to compel agency action under 5 U.S.C. § 706(1), "agencies could effectively prevent judicial review of their policy determinations by simply refusing to take final action."). It is especially pernicious that FDA has attempted to flip the burden onto a drug manufacturer to obtain a final order that is subject to judicial review; but the statute, by contrast, *obligates* FDA to provide a notice of an opportunity for a hearing if it does not approve an NDA.

6. Beyond its regulations, FDA has adopted a routine practice of disregarding its statutory obligations. The Prescription Drug User Fee Act (PDUFA) authorizes FDA to collect fees from drug companies—funds that must be "dedicated toward expediting the review of human drug applications." *See* Pub. L. No. 102-571, 106 Stat. 4491 (1992); 21 U.S.C. § 379g note. Nevertheless, FDA's performance "goal" under PDUFA for a standard NDA is to "[r]eview and act on 90 percent of [applications] within 10 months of the 60-day filing date." FDA, *PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027* at 4 (last visited Feb. 4, 2024), https://www.fda.gov/media/151712/download. That is, FDA's own "goal" for responding to NDAs is approximately *360* days (assuming 30 days in each month, plus 60 days from when the applicant submits the NDA) or *double* the amount of time mandated by Congress. The FDA effectively admits that it has no intention of following the statutory deadline for the majority of NDAs, despite the fact that it collects more than $4,000,000 in fees for each new application requiring clinical data, and the fact that FDA based that fee amount on its own assessment of its "resource capacity needs" to review NDAs. *Vanda Pharms.*, 2024 WL 307387, at *6 (quoting *Prescription Drug User Fee Rates for FY 2024*, 88 Fed. Reg. 48,881, 48,882 (2023)). As another court in this District already found, "with higher funds comes higher expectations," and given the additional funds available to FDA, the "unreasonableness in agency's

delay comes sooner than it did prior to the PDUFA." *Sandoz, Inc. v. Leavitt*, 427 F. Supp. 2d 29, 40 (D.D.C. 2006).

7. To be sure, there *is* a mechanism by which FDA *will* comply with its statutory obligation—FDA's priority review voucher (PRV) system. Under the program, sponsors can obtain a voucher that guarantees FDA will review a sponsor's chosen new drug application within 6 months—that is, the same 180 days the statute already requires. Once obtained from FDA for a fee of approximately $1.3 million, the voucher is transferrable, and if sold, can be redeemed by the new owner to obtain this expedited review. A report from the GAO indicated that the value of sales of the vouchers ranged from $67.5 to $350 million. Other recent reported sales of vouchers have been approximately $100 million. The fact that pharmaceutical companies are willing to pay tens or hundreds of millions of dollars to obtain timely review from FDA—the period of review mandated by the statute—reinforces the significant harms that FDA's practice inflict on pharmaceutical innovators. What is more, that FDA *will* timely review an application if a priority review voucher is used is proof positive that FDA *can* achieve the statutory deadline—and that it has simply chosen not to in the majority of cases.

8. Vanda is a small pharmaceutical company focused on the development and commercialization of innovative therapies to address high-priority unmet medical needs and improve the lives of patients. One of those therapies is Hetlioz® (tasimelteon)—the first drug that FDA approved to treat two different rare conditions: Non-24-Hour Sleep-Wake Disorder (Non-24), a debilitating circadian-rhythm disorder that disproportionately afflicts individuals who are totally blind, and nighttime sleep disturbances in individuals with Smith-Magenis Syndrome, a rare genetic neurodevelopment disorder. Because Vanda is devoted to developing and commercializing innovative new treatments, Vanda must make significant investments in research and development in order to commercialize new therapies.

9. This case concerns Vanda's supplemental NDA for Hetlioz® to treat insomnia characterized by difficulties with sleep initiation, the product of years of hard work, research, and development. Vanda submitted its Hetlioz® insomnia sNDA to FDA on May 4, 2023. Vanda has not received approval or a notice of opportunity for a hearing as of the date of this complaint, 278 days later. Thus, there can be no dispute that FDA has failed to process the sNDA within the time frame mandated by Congress. The statutory deadlines are critical to ensuring not only that manufacturers' time-limited patent rights over their drugs are not eroded by significant bureaucratic delay in approval, but also that patient access to new and promising therapies is not slowed by government red tape.

10. Because FDA has unlawfully withheld agency action, the Court should "compel" FDA to act on Vanda's sNDAs pursuant to 5 U.S.C. § 706(1). And, because FDA's regulations directly conflict with the mandatory deadlines set by Congress, the Court should declare them a nullity pursuant to 5 U.S.C. § 706(2).

PARTIES

11. Plaintiff Vanda Pharmaceuticals Inc. is a global biopharmaceutical company focused on the development and commercialization of innovative therapies to address high-priority unmet medical needs and to improve the lives of patients. Vanda is incorporated in Delaware and maintains its principal place of business in Washington, D.C.

12. Defendant Food and Drug Administration is an agency of the United States government within the Department of Health and Human Services. The Secretary of Health and Human Services has delegated to FDA the authority to administer the relevant provisions of the Food, Drug, and Cosmetic Act, 21 U.S.C. § 301 *et seq*. FDA is headquartered in Silver Spring, Maryland.

13. Defendant Robert M. Califf, M.D., is Commissioner of Food and Drugs. The Commissioner of Food and Drugs has delegated authority to administer the FDCA. He is sued in his official capacity only.

14. Defendant Department of Health and Human Services (HHS) is a cabinet-level executive department charged with enhancing the health and well-being of all Americans. FDA is an agency of the United States government within HHS. HHS is headquartered in Washington, DC.

15. Defendant Xavier Becerra is Secretary of Health and Human Services. He is the official charged by law with administering the FDCA. He is sued in his official capacity only.

JURISDICTION AND VENUE

16. Vanda brings this suit under the Administrative Procedure Act, 5 U.S.C. §§ 551 *et seq.*, the Declaratory Judgment Act, 28 U.S.C. § 2201, the Mandamus Act, 28 U.S.C. § 1361, and the All Writs Act, 28 U.S.C. § 1651.

17. This case arises under the laws of the United States. The court's jurisdiction is thus invoked under 28 U.S.C. § 1331. This court also has jurisdiction under the Mandamus Act, 28 U.S.C. § 1361.

18. Venue is proper in this district under 28 U.S.C. § 1391(e) because Plaintiff Vanda resides in this district, and no real property is involved in this action.

FACTUAL ALLEGATIONS

A. Statutory and Regulatory Background

19. The FDCA sets out a comprehensive scheme for federal government approval of newly developed drugs, and it prohibits the introduction into interstate commerce of any new drug absent approval of a new drug application (NDA). *See* 21 U.S.C. § 355(a).

20. The FDCA includes a mandatory timeframe for action on a drug manufacturer's NDA. Specifically, the statute provides that "[w]ithin one hundred and eighty days after the filing

of an [NDA], or such additional period as may be agreed upon by the [FDA] and the applicant, the [FDA] shall either—(A) approve the application . . . or (B) give the applicant notice of an opportunity for a hearing." 21 U.S.C. § 355(c)(1).

21. This same timeline applies to action on a supplemental new drug application (sNDA), which is the mechanism through which the manufacturer of an already approved drug may seek approval for an additional indication—that is, approval of the same drug to treat a different condition. *See generally* 21 C.F.R. § 314.70.

22. Despite these clear statutory deadlines, FDA regulations purport to suspend the 180-day deadline during any period after the agency sends the applicant a "complete response letter" identifying problems with the NDA, and before the applicant takes one of a list of specified actions, including formally requesting an opportunity for a hearing. 21 C.F.R. § 314.110(b), (c). Specifically, when the agency issues a complete response letter, the applicant is given one year to take one of three specified actions: "[r]esubmit the application . . . addressing all deficiencies identified"; "[w]ithdraw the application"; or affirmatively "[r]equest opportunity for hearing." 21 C.F.R. § 314.110(b)(1)-(3). Importantly here, the same regulation declares unilaterally that "[a]n applicant *agrees* to extend the review period under [21 U.S.C. § 355(c)(1)] until it takes" one of these three actions. 21 C.F.R. § 314.110(c)(1) (emphasis added).

23. The regulations further provide that once the applicant does request an opportunity for a hearing, FDA "will either approve the application . . . , or refuse to approve the application . . . and give the applicant written notice of an opportunity for a hearing" "[w]ithin 60 days of the date of the request for an opportunity for a hearing." *Id.* § 314.110(b)(3).

24. FDA also purports to extend the 180-day deadline by giving itself an additional 60 days at the beginning of the process to determine whether an application can be "filed." Instead of deeming an NDA or sNDA filed on the date it is submitted by the applicant, FDA deems NDAs filed "60 days after the date FDA received the NDA." 21 C.F.R. § 314.101. If FDA determines the

application is complete enough to permit substantive review by the agency, FDA starts the 180-day clock. *See id.* § 314.101(a)(2) ("The date of filing will be the date 60 days after the date FDA received the NDA. The date of filing begins the 180–day period described in section 505(c) of the Federal Food, Drug, and Cosmetic Act.").

B. Factual Background

25. Vanda develops and markets innovative pharmaceutical products to address high-impact unmet patient needs. One of its drugs is Hetlioz® (tasimelteon), a circadian-rhythm regulator that is currently approved by FDA to treat a condition called Non-24, a circadian rhythm disorder in which a patient's internal clock is mismatched to the 24-hour day/night cycle. Hetlioz® is also the first and only FDA-approved treatment for nighttime sleep disturbances in Smith-Magenis Syndrome (SMS), a rare genetic disorder.

26. Vanda is also studying tasimelteon to treat other conditions, including insomnia. Vanda completed substantial studies demonstrating tasimelteon's effectiveness in treating insomnia characterized by difficulties with sleep initiation. Vanda submitted this information, along with significant safety data, to FDA in its Hetlioz® insomnia sNDA on May 4, 2023. FDA deemed the sNDA filed on July 3, 2023. *See* 21 C.F.R. § 314.101(a) (providing that NDAs are deemed filed "60 days after the date FDA received the NDA").

27. In its insomnia sNDA cover letter, Vanda specifically emphasized the agency's 180-day obligation, stating that "Vanda expects FDA to complete review of this application within 180 days of its filing, at which point Vanda expects either approval or notice of an opportunity of a hearing before the Commissioner."

28. 180 days after Vanda submitted its sNDA was October 31, 2023. Vanda did not receive approval or a notice of opportunity for a hearing on its sNDA on that date, and Vanda still has not received the required notice. As of the date of this complaint, it has been 278 days since

the sNDA was submitted, and the FDA has not approved the application or provided a notice of an opportunity for a hearing.

29. Even calculated in light of FDA's own unlawful regulations—which purport to give the agency an extra-statutory 60 days to determine whether the sNDA will be "filed" or refused (21 C.F.R. § 314.101)—180 days after that deemed "filing" date was December 30, 2023. As of the date of this complaint, it has been 218 days since the sNDA was deemed filed, and the FDA has not approved the application or provided a notice of an opportunity for a hearing.

30. On February 4, 2024—FDA's self-selected deadline for communicating labeling changes and anticipated postmarketing requirements—Vanda received a letter from FDA refusing to provide this information "at this time" because of "deficiencies that preclude discussion." FDA provided no further elaboration of its reasons for the letter, leaving Vanda to guess as to what the problem could be, and unable to reasonably respond or engage with the FDA to cure any "deficiencies." It is a "fundamental requirement of administrative law . . . that an agency set forth its reasons for decision; an agency's failure to do so constitutes arbitrary and capricious agency action." *Amerijet Int'l, Inc. v. Pistole*, 753 F.3d 1343, 1350 (D.C. Cir. 2014) (citation and quotation marks omitted). In other words, FDA has apparently decided that something will preclude it from approving Vanda's sNDA yet declined to give Vanda any explanation for this decision. Decisions like this telegraphing FDA's views can have a substantial effect on a company, yet FDA insulates itself from scrutiny by not providing any reasons and, instead, as the letter contemplates, continuing to delay well past statutory deadlines before giving Vanda its notice of an opportunity for a hearing.

C. FDA's Failure to Act is Unlawful

31. By statute, FDA must act on an sNDA by either approving the application or publishing a notice of opportunity for a hearing. The FDCA unambiguously provides that "[w]ithin one hundred and eighty days after the filing of an application …, the Secretary *shall* either … (A)

approve the application … or (B) give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) on the question whether such application is approvable." 21 U.S.C. § 355(c)(1) (emphasis added). The only exception to the 180-day deadline is where an "additional period" is "agreed upon by the Secretary and the applicant." *Id.*

32. The word "'shall' is 'mandatory'" and "usually connotes a requirement." *Kingdomware Techs., Inc. v. United States*, 579 U.S. 162, 171-172 (2016) (quoting *Lexecon Inc. v. Milberg Weiss Bershad Hynes & Lerach*, 523 U.S. 26, 35 (1998)). In particular, "[w]hen a statute distinguishes between 'may' and 'shall'"—as Section 355 frequently does— "it is generally clear that 'shall' imposes a mandatory duty." *Id*. at 172; *see also Me. Cmty. Health Options v. United States*, 140 S. Ct. 1308, 1320 (2020) (statutory term "shall" is "mandatory language" that "typically creates an obligation impervious to discretion") (quotation marks omitted, alteration incorporated). This Court has previously held that the FDCA's "180-day statutory provision imposes a mandatory obligation on the FDA," and as such, FDA "is required to take action on [an applicant's] NDA within 180 days of its filing." *Sandoz, Inc.*, 427 F. Supp. 2d at 33-38; *see also id.* at 34 (rejecting FDA's argument that PDUFA rendered the 180-day deadline "aspirational rather than mandatory"); *see also In re Barr Lab'ys, Inc*., 930 F.2d 72, 74 (D.C. Cir. 1991) (concluding identical statutory language in § 355(j)(5)(A) to be a "facially mandatory statutory deadline").

33. Moreover, due to FDA's regulations that purport to supplant the statutory deadlines Congress enacted, FDA almost always concludes its review of new drug applications with a complete response letter instead of a final denial, meaning that FDA has effectively insulated itself from judicial review of its decisionmaking. *See Nostrum Pharms.*, 35 F.4th at 826 (holding that a complete response letter is not a final agency action entitled to judicial review). An agency should not be able to escape judicial review, however, by "delaying [its] determination indefinitely." *See Environmental Defense Fund*, 439 F.2d at 593; *see Cobell*, 240 F.3d at 1095 (noting that, without

the court's ability to compel agency action under 5 U.S.C. § 706(1), "agencies could effectively prevent judicial review of their policy determinations by simply refusing to take final action."). This is contrary to the basic presumption of judicial review embodied in the APA and the Constitution. *See Lincoln v. Vigil*, 508 U.S. 182, 190 (1993) (the Supreme Court has "read the APA as embodying a basic presumption of judicial review" (citations and quotation marks omitted)); *see* S. Rep. 79-752, at 212 ("It has never been the policy of Congress to prevent the administration of its own statutes from being judicially confined to the scope of authority granted or to the objectives specified."). An agency's attempt to delay final action to avoid judicial review thus subverts traditional separation of powers principles: Congress enacts legislation, the Executive implements it, and Judiciary ensures faithful compliance to Congress's legislative commands.

34. There can be no debate that FDA has not acted within 180 days here. It has been 278 days since Vanda's sNDA was submitted, and the FDA has not approved the application or provided a notice of an opportunity for a hearing. Moreover, even granting FDA its extra-statutory 60 additional days, FDA is still well past the deadline.

35. Thus, FDA has an obligation to immediately respond to the sNDA via either an approval or a notice of opportunity for a hearing. The Court should issue a declaratory judgment that FDA's delay is unlawful—indeed, it is critical for the Court to so determine, as FDA has demonstrated no intention to act in a timely manner otherwise.

D. FDA's Regulations Are Contrary to Law and Must Be Set Aside

36. As noted above, FDA's complete response letter regulations purport to extend the statutorily mandated deadline for providing either approval or a notice of opportunity for a hearing. Adopted in 2008, those regulations provide that, rather than giving the notice of opportunity for hearing required by statute, at or before the 180-day mark, FDA instead "will send the applicant a complete response letter if the agency determines that we will not approve the application . . . in

its present form." 21 C.F.R. § 314.110(a). The regulations then give the applicant three options: (1) "[r]esubmission" of the NDA, "addressing all deficiencies identified in the complete response letter"; (2) "[w]ithdrawal" of the application; or (3) that the applicant must request the opportunity for a hearing guaranteed by statute. *Id*. § 314.110(b)(1)-(3). And even when the applicant "request[s]" the "opportunity for a hearing," the regulations purport to give FDA 60 *more* days before it must issue the notice of opportunity for a hearing. *Id.* § 314.110(b)(3). The regulations further assert that "[a]n applicant agrees to extend the review period under [21 U.S.C. § 355(c)(1)] until it takes any of the actions" just listed. 21 C.F.R. § 314.110(c).

37. A regulation that is inconsistent with a statute is void. *See, e.g.*, *NAACP v. DeVos*, 485 F. Supp. 3d 136, 145 (D.D.C. 2020) ("The authority to issue regulations is not the power to make law, and a regulation contrary to a statute is void.") (quoting *Orion Reserves Ltd. P'ship v. Salazar*, 553 F.3d 697, 703 (D.C. Cir. 2009)). By purporting to allow the agency to avoid its statutory deadline for action, the complete response letter regulations conflict with the statute, and are therefore a nullity. *Id.*; *see also Texas v. EPA*, 726 F.3d 180, 195 (D.C. Cir. 2013) (Kavanaugh, J.) ("A valid statute always prevails over a conflicting regulation, and a regulation can never trump the plain meaning of a statute.") (quotation marks and citation omitted; alteration incorporated).

38. FDA's regulations are flatly inconsistent with the governing statute, which imposes a mandatory obligation on the agency to take a certain action (approve the NDA or issue a notice of opportunity for hearing) within a specified time (180 days). Nowhere does the statute mention this third option the FDA has invented, and FDA's inclusion in the regulations of at *least* 60 additional days of delay by requiring an applicant to "request" the opportunity for hearing is irreconcilable with the statutory scheme. The regulation is therefore invalid and must be set aside.

39. Nor is the regulation's flat assertion that "[a]n applicant agrees to extend" FDA's statutory deadline "until [the applicant] takes" specified action (21 C.F.R. § 314.110(c)) a legitimate application of the statute's requirement that the deadline "shall" be either 180 days "or

such additional period as may be agreed upon by the [FDA] and the applicant." 21 U.S.C. § 355(c)(1). Under fundamental principles of contract law, an "agree[ment]" (*id.*) both "requires a bargain in which there is a manifestation of mutual assent" (Restatement (Second) of Contracts § 17)—that is, it cannot be created by one party unilaterally—and cannot exist absent bargained-for consideration (*id.* § 71), which is also lacking here, where the applicant gains nothing from purportedly absolving FDA from its statutory deadline. *See, e.g.*, *United States v. Honeywell Int'l, Inc.*, 47 F. 4th 805, 813 (D.C. Cir. 2022) (courts "presume Congress employs common law terms with their common law meaning, absent a contrary indication in the statute"); *cf. also* Restatement (Second) of Contracts § 177 (providing that where one "party's manifestation of assent is induced by undue influence by the other party, the contract is voidable by the victim").

40. In addition, FDA's regulations purport to give the agency another *additional* 60 days upfront to determine whether an application can be deemed "filed." *See* 21 U.S.C. § 314.101. This is also inconsistent with the plain text of the FDCA and must be set aside.

41. The statute provides that "[a]ny person may file with the Secretary an application with respect to any drug." 21 U.S.C. § 355(b)(1). The statute further provides that "[w]ithin one hundred and eighty days after *the filing* of an application under subsection (b) . . . the Secretary shall either —(A) approve the application . . . or (B) give the applicant notice of an opportunity for a hearing." 21 U.S.C. § 355(c)(1) (emphasis added). The only exception to this deadline is when an "additional period" is "agreed upon by the Secretary and the applicant." *Id*.

42. FDA regulations, however, provide that an NDA (or sNDA) is not "filed" when the FDA receives it; rather, the agency has "60 days" from receipt to "determine whether the NDA may be filed." 21 C.F.R. § 314.101(a)(1). The regulations further provide that the "date of filing will be the date 60 days after the date FDA received the NDA" and this new "filing" date "begins the 180–day period described in section 505(c) of the Federal Food, Drug, and Cosmetic Act." *Id.* § 314.101(a)(2).

43. When interpreting statutes, the court "begin[s] 'where all such inquiries must begin: with the language of the statute itself.'" *Republic of Sudan v. Harrison*, 139 S. Ct. 1048, 1056 (2019) (quoting *Caraco Pharm. Lab'ys, Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 412 (2012)). The term "file" in this context most naturally means "to initiate . . . through proper formal procedure." *See File*, Merriam-Webster Dictionary, perma.cc/6XED-6B6D (last viewed Jan. 15, 2024). More importantly, under the statute, the *applicant* files the NDA, not the Secretary. *See* 21 U.S.C. § 355(b)(1). The statute makes no mention of any procedure by which the Secretary determines whether or not an application "may be filed" before the 180-day review period begins.

44. Thus, the most natural and unambiguous understanding of the text of § 355(c) is that the 180-day period runs from the date the applicant filed the NDA. FDA's contrary regulations, which extend this period an additional 60 days, are null and void.

45. Indeed, FDA's own policy statements seem to acknowledge that these two regulations extend the statutory 180-day period. In 2021, HHS rescinded a policy statement that would have required FDA to annually publish data on its website for each NDA and ANDA that included the date the NDA was filed and the total days in excess of 180 days for approval. FDA, *Withdrawal of Notice Regarding the Food and Drug Administration Drug Review Timeline Transparency; Revocation of Statement of Policy*, 86 Fed. Reg. 23,389, 23,389 (May 3, 2021). In the withdrawal notice, FDA said the prior policy statement "did not take into account all of the relevant considerations related to the timeframe for FDA's review of drug applications," which include (1) the fact that FDA regulations add an additional 60 days before the 180-day review period starts, (2) the 180-day review period can be "extended" when FDA issues a complete response letter, and (3) the agency regularly meets or exceeds its PDUFA goals (which are, of course, much longer than the statutory mandate). *Id.* at 23,390. Thus, not only does FDA recognize that these two regulations extend the 180-day review period, but FDA also treats its PDUFA goals as the real timeline for review, despite the contrary ruling in *Sandoz*, 427 F. Supp. at 35-37.

46. All told, FDA's regulations combine to purport to give FDA at least *120 more days* beyond the statutory 180 days to resolve new drug applications. Nearly doubling the amount of time the statute contemplated is flatly inconsistent with the statute Congress enacted, which was intended to ensure expeditious decisions on new drug applications. FDA has effectively crafted itself a hall pass to ignore congressionally mandated deadlines. But "a regulation contrary to a statute is void," (*NAACP*, 485 F. Supp. 3d at 145) and the Court should set these regulations aside.

47. What is more, FDA's initial adoption of these regulations is inconsistent with the basic requirements of the Appointments Clause. The Constitution requires that the President "shall nominate," with the advice and consent of the Senate, appoint all "Officers of the United States, whose Appointments are not . . . otherwise provided for, and which shall be established by Law," and "Congress may by Law vest the Appointment of such inferior Officers, as they think proper, in the President alone, in the Courts of Law, or in the Heads of Departments." U.S. Const. art. II, § 2, cl. 2. "[A]ny appointee exercising significant authority pursuant to the laws of the United States is an 'Officer of the United States,' and must, therefore, be appointed in the manner prescribed" by the Appointments Clause. *Buckley v. Valeo,* 424 U.S. 1, 126 (1976) (per curiam).

48. The regulations at issue here were signed by Jeffrey Shuren, then the Associate Commissioner for Policy and Planning. 73 Fed. Reg. 39,588, 39,611 (July 10, 2008). So far as Vanda is aware, there is no information in the public record demonstrating that Mr. Shuren was appointed by "the President alone," by a court, or by a "Head[] of Department[]." Const. art. II, § 2, cl. 2; *Lucia v. SEC*, 138 S. Ct. 2044, 2051 n.3 (2018). And he certainly was not appointed by the President or confirmed by the Senate. *See* United States Government Policy and Supporting Positions (Plum Book), 2008, at 72-74, perma.cc/7M2D-5PYM.

49. Even if Mr. Shuren had been appointed by, for example, a Head of Department, he was not a valid Officer because he did not occupy a position whose appointment Congress has "*vest[ed]* . . . in the President alone, in the Courts of Law, or in the Heads of Departments." U.S.

Const. art. II, § 2, cl. 2 (emphasis added). The Appointments Clause makes clear that "[t]he head of a department has no constitutional prerogative of appointment to offices independently of the legislation of congress." *United States v. Perkins*, 116 U.S. 483, 485 (1886). There is no statute which vests appointment authority for Mr. Shuren's position in any of the constitutionally prescribed alternative authorities. This stands in stark contrast to other components of the Department of Health and Human Services. With respect to the Social Security Administration, for example, the Secretary of Health and Human Services is empowered to "appoint and fix the compensation of such *officers* and employees . . . as may be necessary for carrying out the functions of the Secretary under [chapter 7 of Title 42]." 42 U.S.C. § 913 (emphasis added). Nor can general housekeeping statutes provide the necessary authority; the "power to 'keep house' . . . is not the same as the power to 'build the house' by appointing officers." *United States v. Concord Mgmt. & Consulting LLC*, 317 F. Supp. 3d 598, 622 (D.D.C. 2018). Congress has not "vested" authority in the HHS Secretary to appoint officers to the position held by Mr. Shuren. He was thus not appointed pursuant to power vested by Congress in a proper authority, and thus was not a valid Officer.

50. There can be little doubt that promulgation of a binding regulation is the kind of authority that can only be exercised by an Officer. *See Officers of the United States Within the Meaning of the Appointments Clause*, 31 Op. O.L.C. 73, 78, 88 (2007) ("[D]elegated sovereign authority" includes the "power to issue regulations and authoritative legal opinions on behalf of the government.").

51. More concretely, the promulgation of a binding regulation is an action that can only be executed by a *Principal* Officer—which Mr. Shuren was undoubtedly not. The touchstone of the constitutional distinction between the powers of Principal and Inferior Officers is that "[o]nly an officer properly appointed to a principal office may issue a final decision binding the Executive Branch." *United States v. Arthrex*, 141 S. Ct. 1970, 1985 (2021). A rule is certainly final and

binding on the agency. *See Nat'l Envtl. Dev. Ass'n's Clear Air Project v. EPA*, 752 F.3d 999, 1009 (D.C. Cir. 2014) (quoting *Panhandle E. Pipe Line Co. v. FERC*, 613 F.2d 1120, 1135 (D.C. Cir. 1979)) ("It is axiomatic . . . that an agency is bound by its own regulations."). And even under the D.C. Circuit's three-factor test, Mr. Shuren's position requires Principal Officer appointment. *See Intercollegiate Broad. Sys., Inc. v. Copyright Royalty Bd.*, 684 F.3d 1332, 1338 (D.C. Cir. 2012).

52. FDA's previous purported ratification of *all* actions before 2016 does not remedy this Appointments Clause issue. FDA undertook an agency-wide reorganization in 2016 in which Commissioner Califf ratified all actions taken by FDA officials and their subordinates prior to the date of the ratification. This boilerplate ratification—essentially a declaration that there were no Appointments Clause issues at FDA before 2016—cannot carry any weight. Although the D.C. Circuit has recognized that a properly appointed official can ratify more than one decision at a time, (*Wilkes-Barre Hosp. Co., LLC v. NLRB*, 857 F.3d 364, 371 (D.C. Cir. 2017) (upholding Board ratification of administrative and personnel actions for an approximately 18-month period)) and suggested that the review of a prior decision can be a "rubberstamp," (*id.* at 372), it is still a basic requirement of proper ratification that "a properly appointed official has the power to conduct an independent evaluation of the merits *and does so*." *Intercollegiate Broad. Sys. v. Copyright Royalty Bd.*, 796 F.3d 111, 117-121 (D.C. Cir. 2015) (emphasis added). It is inconceivable to think that Commissioner Califf was able to actually evaluate, and *did* evaluate, even if cursorily, any and all actions taken by his delegees or their subordinates for all time prior to September 2016, which is what the blanket ratification purported to do.

E. The Court Should Compel FDA to Act

53. FDA's failure to abide by its mandatory obligations—under the FDCA and its own regulations—to act on Vanda's sNDA within 180 days is unlawful and warrants the issuance of a writ of mandamus and/or relief under 5 U.S.C. § 706(1) to "compel agency action unlawfully withheld or unreasonably delayed." The legal analysis for both forms of relief is the same: analysis

under the *TRAC* factors. *See, e.g.*, *Bagherian v. Pompeo*, 442 F. Supp. 3d 87, 96 (D.D.C. 2020) ("The standard by which a court reviews agency inaction is the same under both § 706(1) of the APA and the Mandamus Act.") (quotation marks omitted; alteration incorporated).

54. In *TRAC*, the D.C. Circuit set out a number of factors that govern claims of unreasonable agency delay:

1. the time agencies take to make decisions must be governed by a rule of reason;
2. where Congress has provided a timetable or other indication of the speed with which it expects the agency to proceed in the enabling statute, that statutory scheme may supply content for this rule of reason;
3. delays that might be reasonable in the sphere of economic regulation are less tolerable when human health and welfare are at stake;
4. the court should consider the effect of expediting delayed action on agency activities of a higher or competing priority;
5. the court should also take into account the nature and extent of the interests prejudiced by delay; and
6. the court need not find any impropriety lurking behind agency lassitude in order to hold that agency action is unreasonably delayed.

Telecommunications Rsch. & Action Ctr. v. FCC, 750 F.2d 70, 79-80 (D.C. Cir. 1984) (*TRAC*).

55. Those factors are satisfied here. *See, e.g.*, *Sandoz*, 427 F. Supp. 2d at 33-41 (finding FDA's noncompliance with the 180-day deadline for NDAs unlawful, and compelling FDA action pursuant to 5 U.S.C. § 706(1)); *Vanda Pharms.*, 2024 WL 307387, at *3 (noting that "Congress. . . provided a timetable here that the agency acknowledges it has exceeded" and ordering FDA to act on Vanda's application under 5 U.S.C. § 706(1)). In particular, the FDCA's 180-day deadline for response to an NDA is both binding and judicially cognizable (*see Sandoz*, 427 F. Supp. 2d at 34-38), and the agency's routine delays are "egregious" (*id.* at 40). Moreover, FDA routinely flouts

this obligation. According to one recent agency analysis of NDA approvals in 2019, the average time between submission and approval was 273.8 days. *See FDA Drug Review Timeline Transparency; Statement of Policy,* 86 Fed. Reg. 4,083, 4,084 (Jan. 15, 2021). And FDA's own self-selected "goal" under the PDUFA of taking action on standard NDAs within 10 months of the filing date similarly openly disregards the statutory deadline.

56. FDA's complete response letter regulations do not absolve the agency of its statutory responsibility to act by approving the NDA or giving notice of an opportunity for hearing within 180 days. *See* 21 U.S.C. § 355(c)(1). As noted above, those regulations are void as inconsistent with the FDA's governing statute, and therefore cannot provide a legitimate basis for an agency's action (or failure to act). *See, e.g.*, *NAACP*, 485 F. Supp. 3d at 145 ("The authority to issue regulations is not the power to make law, and a regulation contrary to a statute is void.") (quoting *Orion*, 553 F.3d at 703).

57. Nor is the regulation's flat assertion that "[a]n applicant agrees to extend" FDA's statutory deadline "until [the applicant] takes" specified action (21 C.F.R. § 314.110(c)) a legitimate application of the FDCA's provision that the deadline "shall" be either 180 days "or such additional period as may be agreed upon by [FDA] and the applicant." 21 U.S.C. § 355(c)(1). Because there was no legitimate "agree[ment]" (21 U.S.C. § 355(c)(1)) between FDA and Vanda to extend FDA's statutory deadline to act, that deadline has long since passed, notwithstanding anything to the contrary in the complete response letter regulations. *See, e.g.*, *NAACP*, 485 F. Supp. 3d at 145. As in *Sandoz*, therefore, FDA's inaction on Vanda's sNDAs warrants APA and mandamus relief.

58. The seriousness of FDA's delay is further underscored by the priority review voucher program. Under said program, sponsors of certain types of drugs—those that treat tropical diseases, rare pediatric diseases, and medical countermeasures to national security threats—are eligible to receive a "priority review voucher" (for a fee of approximately $1.3 million paid to

FDA) that can be redeemed with the submission of a future drug application. *See, e.g.*, 21 U.S.C. § 360ff; FDA, *Fee Rate for Using a Priority Review Voucher in Fiscal Year 2024*, 88 Fed. Reg. 67,305, 67,306 (Sept. 29, 2023). The voucher guarantees FDA will act on that application within six months—that is, the same 180 days the statute already requires. The vouchers are transferrable and can then redeemed by the new owner to obtain this expedited review. A recent GAO report reviewed prior sales of priority review vouchers and determined that the sale value ranged between $67.5 to $350 million. *See* Gov't Accountability Office, *Drug Development: FDA's Priority Review Voucher Programs* (Jan. 2020), perma.cc/69AZ-WN46. Recent sales of priority review vouchers have garnered similarly high prices. For example, in July 2022 Novartis purchased a priority review voucher from Mallinckrodt for $100 million, and in February 2022 BioMarin sold a priority review voucher for $110 million.[2] The fact that pharmaceutical companies are willing to pay tens or hundreds of millions of dollars to obtain timely review from FDA only reinforces the significant harm Vanda has suffered as a result of the agency's extraordinary delay here.

59. Finally, this case is an appropriate instance for the Court to exercise its equitable powers to enforce the statutory deadline. Unlike the situation that confronted the D.C. Circuit in *In re Barr*, 930 F.2d 72, the material circumstances within FDA are substantially different now. As this Court noted in *Sandoz*, FDA's funding drought, which was "a driving force behind the FDA's delay" in *In re Barr*, was ameliorated by Congress when it enacted PDUFA. *Sandoz*, 427 F. Supp. 2d at 40. "With additional funds now available to the FDA for its processing of NDAs, unreasonableness in agency's delay comes sooner than it did prior to the PDUFA." *Id.* Moreover, as the Court also recognized, mandamus here does not "necessarily require that the agency formulate its final decision," rather, the agency can (and indeed must) offer Vanda the notice of

[2] Angus Liu, *Novartis Buys FDA Priority Review Voucher from Bankrupt Mallinckrodt for $100M*, FiercePharma (July 1, 2022), perma.cc/MW76-Z7S8.

opportunity for hearing to which it is entitled under the statute. *Id.* at 39 n.11. Thus, the concerns that animated the court in *In re Barr* about allocation of agency resources are not implicated here.

60. In sum, the FDA must abide by the mandatory timeframes imposed by statute and binding regulation. Moreover, FDA's unlawful delays continue to grow, heightening the need for relief. Mandamus is therefore warranted to compel the action required under the FDCA and its implementing regulations: to either approve Vanda's sNDAs or provide notice in the Federal Register of opportunity for a hearing.

CLAIMS FOR RELIEF
COUNT I
ADMINISTRATIVE PROCEDURE ACT, 5 U.S.C. § 706(1)

61. Vanda incorporates and re-alleges the foregoing paragraphs as though fully set forth herein.

62. The APA empowers courts to "compel agency action unlawfully withheld or unreasonably delayed." 5 U.S.C. § 706(1).

63. The FDCA imposes a nondiscretionary duty on FDA to either "approve" Vanda's sNDA or "give [Vanda] notice of an opportunity for a hearing" in the Federal Register "[w]ithin one hundred and eighty days after the filing of" the sNDA (21 U.S.C. § 355(c)(1); *see* 21 C.F.R. § 314.200(a)(2)), but it has now been 278 days since Vanda submitted the insomnia sNDA, and the agency has still not acted.

64. The factors laid out by the D.C. Circuit in *TRAC*, 750 F.2d 70, warrant relief.

65. The Court should therefore "compel" FDA to act on Vanda's sNDAs pursuant to 5 U.S.C. § 706(1) by either approving the sNDAs or publishing notice of an opportunity for hearing in the Federal Register.

COUNT II
MANDAMUS ACT, 28 U.S.C. § 1361

66. Vanda incorporates and re-alleges the foregoing paragraphs as though fully set forth herein.

67. The Mandamus Act provides that "[t]he district courts shall have original jurisdiction of any action in the nature of mandamus to compel an officer . . . of the United States or any agency thereof to perform a duty owed to the plaintiff." 28 U.S.C. § 1361; *see also id.* § 1651 (All Writs Act, providing that courts "may issue all writs necessary or appropriate in aid of their respective jurisdictions and agreeable to the usages and principles of law").

68. The FDCA imposes a nondiscretionary duty on FDA to either "approve" Vanda's sNDA or "give [Vanda] notice of an opportunity for a hearing" in the Federal Register "[w]ithin one hundred and eighty days after the filing of" the sNDA (21 U.S.C. § 355(c)(1); *see* 21 C.F.R. § 314.200(a)(2)), but it has now been 278 days since Vanda submitted the insomnia sNDA, and the agency has still not acted.

69. The factors laid out by the D.C. Circuit in *TRAC*, 750 F.2d 70, warrant relief.

70. The Court should therefore issue a writ of mandamus compelling FDA to act on Vanda's sNDAs by either approving the sNDAs or publishing notice of an opportunity for hearing in the Federal Register.

COUNT III
ADMINISTRATIVE PROCEDURE ACT, 5 U.S.C. § 706(2)

71. Vanda incorporates and re-alleges the foregoing paragraphs as though fully set forth herein.

72. The APA authorizes courts to set aside agency action that is contrary to law. 5 U.S.C. § 706(2).

73. An agency regulation "contrary to a statute is void." *Orion*, 553 F.3d at 703; *see also Texas v. EPA*, 726 F.3d at 195 ("A valid statute always prevails over a conflicting regulation, and a regulation can never trump the plain meaning of a statute").

74. FDA's regulations that purport to extend deadline for the agency to either approve the application or provide a notice of opportunity for a hearing are contrary to the plain text of the governing statute, 21 U.S.C. § 355.

75. The 60-day "filing" regulations are contrary to the statute because the FDA uses them to dramatically extend the statutory deadline. By not deeming an application "filed" until 60 days after the applicant submits it, FDA affords itself 60 extra days beyond what Congress mandated. This is irreconcilable with the statutory scheme.

76. The complete response letter regulations are contrary to the statute in two ways. *First*, the complete response letter regulations contemplate that FDA "will issue" a complete response letter instead of the notice of an opportunity for a hearing that the statute contemplates. *Second*, the complete response letter regulations introduce delay unlawfully, contrary to the statutory 180 days. The complete response letter regulations permit at least *60* additional days of delay after an applicant "requests" the opportunity for a hearing and mandates that the applicant has agreed to this delay. This scheme is irreconcilable with the statutory timeframe.

77. The complete response letter regulations are also invalid because they were not signed by a principal officer of the United States, as required by the Appointments Clause of the U.S. Constitution. *See* U.S. Const. art. II, § 2, cl. 2. They are further unlawful because it does not appear that they were signed by a validly appointed officer of the United States *at all*.

78. Because FDA's regulations are contrary to the statutory text and were invalidly promulgated, those regulations must be set aside. *See, e.g.*, *Decker v. Nw. Envtl. Def. Ctr.*, 568 U.S. 597, 609 (2013) ("It is a basic tenet that 'regulations, in order to be valid, must be consistent

with the statute under which they are promulgated.'" (quoting *United States v. Larionoff,* 431 U.S. 864, 873 (1977))).

COUNT IV
DECLARATORY JUDGMENT ACT, 28 U.S.C. § 2201

79. Vanda incorporates and re-alleges the foregoing paragraphs as though fully set forth herein.

80. The Declaratory Judgment Act provides that, "[i]n a case of actual controversy within its jurisdiction . . . any court of the United States, upon the filing of an appropriate pleading, may declare the rights and other legal relations of any interested party seeking such declaration." 28 U.S.C. § 2201(a).

81. As described above, there is an actual controversy between Vanda and the FDA that is within this Court's jurisdiction.

82. Vanda therefore requests, in addition to mandamus and APA relief, that the Court issue a declaratory judgment declaring that FDA's failure to timely approve or issue a notice of opportunity for hearing violates the statutory timeframes imposed by the FDCA; that the 60-day filing regulation is unlawful; and that the complete response letter regulations are unlawful.

83. Among other reasons, these regulations are invalid because they are incompatible with the governing statutory text and, further, because they were promulgated in violation of the Appointments Clause.

PRAYER FOR RELIEF

WHEREFORE, Vanda respectfully requests that the Court enter judgment in its favor and that the Court:

1. Declare that FDA's lack of compliance with its statutory obligation to act on Vanda's sNDAs within 180 days violates the FDCA;

2. "[C]ompel" FDA to comply with its statutory obligation to act on Vanda's sNDA within 180 days pursuant to 5 U.S.C. § 706(1);
3. Issue a writ of mandamus requiring FDA to comply with its obligation to act on Vanda's sNDAs within 180 days;
4. Declare that FDA's 60-day filing regulation and its complete response letter regulations are unlawful and void; and
5. Award Vanda such other and further relief as the Court may deem just and proper.

Dated: February 6, 2024

Respectfully submitted,

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