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UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

ASCENDIS PHARMA A/S, ASCENDIS PHARMA GROWTH DISORDERS A/S, and ASCENDIS PHARMA, INC.,

Plaintiffs,

v.

BIOMARIN PHARMACEUTICAL INC.,

Defendant.

Case No. 3:25-cv-05696

COMPLAINT FOR DECLARATORY JUDGMENT OF NON-INFRINGEMENT

Plaintiffs Ascendis Pharma A/S, Ascendis Pharma Growth Disorders A/S, and Ascendis Pharma, Inc. (collectively, Ascendis) bring this action against Defendant BioMarin Pharmaceutical Inc. (BioMarin) for a declaratory judgment of non-infringement. Ascendis alleges as follows:

NATURE OF THE CASE

1. This is an action for declaratory judgment that Ascendis does not infringe and has not infringed U.S. Reissue Patent No. 48,267 (RE'267 patent) (attached as Exhibit 1).

2. Ascendis requests declaratory relief because BioMarin has filed a complaint against Ascendis at the U.S. International Trade Commission alleging that Ascendis infringes the RE'267 patent (attached as Exhibit 2). Therefore, there is a present case or controversy between the parties.

3. Ascendis disputes BioMarin's allegations of infringement, and as a result of BioMarin's filing of the ITC complaint, Ascendis is under reasonable apprehension of suit in district court by BioMarin.

PARTIES

4. Ascendis Pharma A/S is a corporation organized and existing under the laws of the Kingdom of Denmark with its registered office and principal executive offices at Tuborg Boulevard 12, DK-2900 Hellerup, Denmark.

5. Ascendis Pharma Growth Disorders A/S is a corporation organized and existing under the laws of the Kingdom of Denmark at Tuborg Boulevard 12, DK-2900 Hellerup, Denmark. Ascendis Pharma Growth Disorders A/S is a wholly-owned subsidiary of Ascendis Pharma A/S.

6. Ascendis Pharma, Inc. is a corporation organized and existing under the laws of Delaware located at 1000 Page Mill Road, Palo Alto, California 94304. Ascendis Pharma, Inc. is a wholly owned subsidiary of Ascendis Pharma A/S.

7. Founded in 2007 and headquartered in Denmark, Ascendis is a global biopharmaceutical company focused on applying its innovative TransCon technology platform by developing TransCon-based therapies to address unmet medical needs for patients throughout the world. Guided by its core values of Patients, Science, and Passion, Ascendis maintains a portfolio of approved Endocrinology Rare Disease products as well as product candidates to address

hypoparathyroidism and growth disorders, such as growth hormone deficiency and, of relevance to the instant action, achondroplasia.

8. On information and belief, BioMarin is a corporation organized and existing under the laws of Delaware with its corporate headquarters, its principal executive offices, and its principal place of business at 770 Lindaro Street, San Rafael, California 94901. BioMarin can be served with process through its registered agent for service, Corporation Service Company, 251 Little Falls Drive, Wilmington, DE 19808.

9. BioMarin has alleged that it is the owner of the RE'267 patent. Exhibit 2 ¶ 28.

JURISDICTION AND VENUE

10. This action arises under the Declaratory Judgment Act, 28 U.S.C. §§ 2201–2202 and under the patent laws of the United States, 35 U.S.C. §§ 1 *et seq.* This Court has subject matter jurisdiction over this action pursuant to 28 U.S.C. §§ 1331 and 1338(a) because this Court has jurisdiction over declaratory judgment claims arising under the patent laws of the United States. *See* 28 U.S.C. §§ 1331, 1338(a), 2201, and 2202.

11. This Court has personal jurisdiction over BioMarin because BioMarin has established minimum contacts with this forum such that the exercise of jurisdiction over BioMarin will not offend traditional notions of fair play and substantial justice. On information and belief, BioMarin does business in this District and maintains its corporate headquarters and principal place of business in this District. Upon information and belief, BioMarin has also been registered to do business in the State of California since at least December 26, 1996. Additionally, on information and belief, BioMarin took actions resulting in the filing of the ITC complaint in this District. *See* Exhibit 2, Ex. 43 (Declaration of Tejas Kheradiva).

12. Venue is proper in this District under 28 U.S.C. §§ 1391 and 1400(b) at least because BioMarin is subject to personal jurisdiction in this District, resides in this District, does business in this District, and maintains its principal place of business in this District. Specifically, BioMarin maintains its corporate headquarters, its principal executive offices, and its principal place of business at 770 Lindaro Street, San Rafael, California 94901. BioMarin lists this address as its global

headquarters on its website. *See* https://www.biomarin.com/contact-us/locations/ (attached as Exhibit 3); *see also* Exhibit 2, Ex. 43 ¶ 9 (asserting that "[t]he San Rafael, California facilities comprise BioMarin's global headquarters").

13. An actual and justiciable controversy exists under 28 U.S.C. §§ 2201–2202 between Ascendis and BioMarin as to whether Ascendis's TransCon CNP investigational prodrug product infringes the RE'267 patent. The controversy is immediate and substantial as reflected by BioMarin's ITC complaint (337-TA-1447) filed before the Commission on April 1, 2025, which asserts that Ascendis is infringing the RE'267 patent.

DIVISIONAL ASSIGNMENT

14. Pursuant to Civil L.R. 3-2(c), 3-5(b), and General Order No. 44, this is an action pertaining to intellectual property rights subject to assignment on a district-wide basis.

EXISTENCE OF AN ACTUAL CONTROVERSY

15. As previously referenced, there is an actual and justiciable controversy within the jurisdiction of this Court under 28 U.S.C. §§ 2201 and 2202.

16. On March 31, 2025, Ascendis submitted a New Drug Application (NDA) to the U.S. Food & Drug Administration for TransCon CNP (navepegritide) for the treatment of children with achondroplasia. *See* Declaration of Annette Bested Toft ¶ 2 (attached as Exhibit 4). Ascendis's TransCon CNP is an investigational prodrug of CNP administered only once weekly. It is specifically designed to treat achondroplasia by allowing for continuous exposure of active CNP to receptors on tissues throughout the body, including growth plates and skeletal muscle.

17. Achondroplasia—also referred to as ACH—is a genetic condition estimated to affect more than 250,000 people worldwide. It is the most common form of skeletal dysplasia. Serious complications and comorbidities stemming from inhibited skeletal development may affect people with achondroplasia, including: sleep apnea, respiratory problems, chronic back and leg pain from lower spine impingement, sudden infant death from brain stem compression, chronic ear infection leading to hearing loss and speech delay, as well as social and emotional challenges experienced by children. The condition is caused by a genetic mutation in the fibroblast growth factor receptor 3

(FGFR-3) resulting in an imbalance between the stimulatory and inhibitory signaling pathways involved in regulating bone growth.

18. C-type natriuretic peptide (CNP)—a naturally occurring peptide that regulates bone growth—has been shown to counteract the FGFR-3 mutation's growth-inhibiting effects and stimulate growth. CNP exists in two major forms *in vivo*, a 53 amino acid peptide, CNP-53 which is the secreted gene product of the CNP (NPPC) gene and is the major endogenous form in tissues, and a 22 amino acid peptide, CNP-22 which is present in very low picomolar concentrations in plasma. In animal models of achondroplasia, continuous exposure of CNP delivered by a transgene was effective in reversing achondroplasia symptoms, and prolonged continuous exposure of CNP is believed to maximize its therapeutic potential.

19. At this stage, Ascendis's TransCon CNP investigational prodrug product has not yet received FDA approval. *See id.* ¶ 2. On June 2, 2025, Ascendis announced that the FDA had accepted for priority review its NDA for TransCon CNP (navepegritide) and had set a Prescription Drug User Fee Act (PDUFA) goal date of November 30, 2025 to complete its review. However, November 30, 2025 is not a date certain by which the FDA will approve the NDA for TransCon CNP (navepegritide) as the FDA may require additional documentation or testing during review.

20. Ascendis has not made, used, offered to sell, sold, or imported its TransCon CNP into the United States, other than for reasons directly related to obtaining FDA approval. Specifically, Ascendis, has had TransCon CNP imported into the United States, solely for use in clinical trials and testing to obtain regulatory approval. *See id.*

21. For all of the drug substance and drug product that has been imported into the United States, the process worked as follows: TransCon CNP drug substance was produced in Europe by Wacker Biotech GmbH. *See id.* ¶ 3. Previously, the aqueous TransCon CNP drug substance was sent to Chicago until 2021, where Vetter Development Services USA Inc. prepared the freeze-dried TransCon CNP drug product and placed the freeze-dried drug product into unlabeled vials. The aqueous drug substance was sent to: Vetter Development Services USA Inc., 8025 Lamon Ave., Skokie, IL 60077. The unlabeled vials with freeze-dried drug product were stored at Vetter in the

United States until shipment to Europe. No aqueous drug substance is left at Vetter in the United States after manufacturing the freeze-dried drug product as only the necessary amount of aqueous drug substance was sent to Vetter for manufacturing the freeze-dried drug product. More recently, Vetter was preparing the freeze-dried TransCon CNP drug product and filling the freeze-dried drug product into vials in Europe. The unlabeled vials with freeze-dried TransCon CNP drug product were then shipped to Fisher Clinical Services in Europe, and Fisher Clinical Services labels the vials and puts them in "kit cartons." Kits are usually packaged with two vials of freeze-dried TransCon CNP drug product. Kits may include prefilled syringes with sterile water for injection (sWFI). These cartons were then sent to clinical testing sites throughout the world. *See id.* For the United States, the cartons were sent to a Fisher U.S. depot for distribution to the clinical sites. The data from all clinical trials conducted anywhere in the world has been or will be reported to the FDA in order to obtain approval. *See id.*

22. The cartons and individual vials sent to the United States have a label that states: "Caution: New Drug – Limited by Federal (or United States) law to investigation use." *See id.* ¶ 4.

23. All of the TransCon CNP that has ever entered into the United States, in any form, is used exclusively to obtain clinical and other testing data that will be provided to the FDA for regulatory approval. *See id.* ¶ 5. Each of these activities are uses reasonably related to the development and submission of information under Federal law, which regulates the manufacture, use, or sale of drugs under 35 U.S.C. § 271(e)(1). In compliance with U.S. law, Ascendis has not sold or offered to sell TransCon CNP in the United States. *See id.* In addition, there have been no sales or offer of sales of TransCon CNP for later importation into the United States. *See id.*

24. Moreover, there have been no excess imported quantities of TransCon CNP into the United States. *See id.* ¶ 6. All TransCon CNP imported into the United States has been used solely for clinical trials and testing to obtain regulatory approval. *See id.* The number of imported vials corresponds to a forecast so that the number of patients enrolled in the trial can be dosed weekly. *See id.* Ascendis only sends the amount of TransCon CNP that is needed to ensure trial patient treatment on a rolling basis. *See id.* Ascendis does not stockpile TransCon CNP in the United States.

See id.

25. On April 1, 2025, the day after Ascendis submitted its NDA to the FDA, BioMarin filed its ITC complaint against Ascendis under Section 337 of the Tariff Act of 1930, as amended, before the Commission. *See* Exhibit 2. BioMarin requested that the Commission institute an investigation to remedy the perceived "unlawful and unfair importation into the United States, and sale for importation into the United States, of certain drug products containing C-type natriuretic peptide ('CNP') variants, and components thereof . . . that infringe, directly and/or indirectly, one or more claims of" the RE'267 patent, specifically independent claims 15 and 18 as well as dependent claims 16–17, 19–20, and 31–48. *Id.* ¶¶ 1–2. BioMarin requests that the Commission issue a permanent limited exclusion order and cease and desist orders against Ascendis. *See id.* § XI (Requested Relief).

26. BioMarin's ITC complaint concedes that Ascendis's TransCon CNP investigational prodrug product is not commercially available and has not yet received FDA approval. *See id.* ¶ 5 (alleging only that "Proposed Ascendis Respondents are prepared to commercially launch a drug product containing C-type natriuretic peptide variants upon FDA approval, which is expected by first quarter 2026"); *id.* ¶ 49 ("if the FDA approves TransCon CNP for the treatment of achondroplasia by the first quarter of 2026") (citations omitted); *id.* ¶ 66 ("Voxzogo® is still the only FDA-approved treatment for achondroplasia for children.") (citations omitted). BioMarin's accompanying Public Interest Statement acknowledges the same. *See* Exhibit 2, Public Interest Statement, at 3 ("have not been approved by the . . . FDA . . . for any indication, but are expected to be used for therapeutic purposes, such as treating achondroplasia in children"); *id.* ("The Accused Products have not established a presence in the U.S. market."); *id.* at 5 ("[A]lthough an NDA has been submitted to the FDA, the Accused Products have not been approved by the FDA and are not currently available to U.S. consumers other than in connection with clinical trials.").

27. Ascendis's TransCon CNP investigational prodrug product does not fall within the scope of the claims of the RE'267 patent. For example, independent claim 15 requires (1) "[a] macromolecule capable of releasing a CNP variant," (2) "a synthetic polymeric group coupled to

the CNP variant through a hydrolysable linkage," and (3) "wherein hydrolysis of the hydrolysable linkage releases the CNP variant." Exhibit 1 at 269:64–270:65. Independent claim 18 requires (1) "[a] sustained release CNP variant formulation" and (2) "a synthetic polymeric group coupled to the CNP variant through a hydrolysable linkage." *Id.* at 271:4–272:5. However, upon information and belief, while the description of "CNP Variant" in the specification of the RE'267 patent includes PEGylated conjugates, it only describes and supports PEGylated conjugates that are *active* in PEGylated form. In contrast, Ascendis's TransCon CNP investigational prodrug product is *inactive* (not functional) in the PEGylated form. Upon further information and belief, "hydrolysis of the hydrolysable linkage" requires hydrolysis through the incorporation of a water molecule. But Ascendis's TransCon CNP investigational prodrug product does not release CNP through hydrolysis. Moreover, the RE'267 patent describes "sustained release" as a composition wherein the CNP variant is "formulated" using "polymeric systems." *See* Exhibit 1 at 88:63–89:7. But Ascendis's TransCon CNP investigational prodrug product is not "formulated" for sustained release using "polymeric systems."

28. BioMarin's allegations to the Commission that there has been a violation of Section 337 based on unfair importation of Ascendis's allegedly infringing TransCon CNP investigational prodrug product establishes the existence of an actual case or controversy.

COUNT I

(Declaratory Judgment of Non-Infringement)

29. Ascendis incorporates by reference and realleges paragraphs 1 through 28 above as if fully set forth herein.

30. BioMarin alleges in its ITC complaint (337-TA-1447) that Ascendis infringes one or more claims of the RE'267 patent through Ascendis's importation of its TransCon CNP investigational prodrug product.

31. The manufacture, use, or importation of Ascendis's TransCon CNP investigational prodrug product has not infringed, and will not infringe, directly or indirectly, any valid and enforceable claim of the RE'267 patent.

32. Accordingly, there exists a controversy of sufficient immediacy and reality to warrant the issuance of a declaratory judgment of non-infringement in the instant action. A judicial declaration is necessary and appropriate so that Ascendis may ascertain its rights regarding its TransCon CNP product in view of the RE'267 patent.

PRAYER FOR RELIEF

WHEREFORE, Ascendis respectfully requests that judgment be entered in its favor and prays that the Court grant the following relief:

A. A judgment declaring that Ascendis has not infringed and is not infringing, either directly or indirectly, any claims of the RE'267 patent;

B. A judgment declaring that Ascendis is the prevailing party and, if the Court determines that this is an exceptional case under 35 U.S.C. § 285, awarding Ascendis its reasonable attorneys' fees, expenses, and costs in connection with this case; and

C. A judgment awarding Ascendis such other relief as the Court may deem just and proper.

Dated: July 7, 2025

/s/ Gabriel S. Gross

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