IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

In re Entresto (Sacubitril/Valsartan) Patent Litigation	Civil Action No. 20-md-2930-RGA
NOVARTIS PHARMACEUTICALS CORPORATION, Plaintiff, v. MSN PHARMACEUTICALS INC., MSN LABORATORIES PRIVATE LIMITED, MSN LIFE SCIENCES PRIVATE LIMITED, GERBERA THERAPEUTICS, INC., and NANJING NORATECH PHARMACEUTICAL CO., LIMITED, Defendants.	Civil Action No. 22-1395-RGA

MEMORANDUM ORDER

Before me is Plaintiff Novartis's motion for preliminary injunction. (D.I. 213).[1] I have considered the parties' briefing. (D.I. 214, 227). I heard oral argument on August 9, 2024.[2]

For the reasons set forth below, this motion is DENIED.

I. BACKGROUND

Novartis holds New Drug Application ("NDA") No. 207620 for Entresto® (sacubitril/valsartan) tablets. (D.I. 1 ¶ 113). Entresto® is indicated "to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart

[1] Docket citations are to Civil Action No. 22-1395 unless otherwise specified.

[2] Citations to the transcript of the argument, which is not yet docketed, are in the format "Hearing Tr. at __."

failure, and for the treatment of symptomatic heart failure with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older." (*Id.*). Several drugmakers, including Defendants MSN Pharmaceuticals Inc., MSN Laboratories Private Limited, and MSN Life Sciences Private Limited (collectively, "MSN"), have filed ANDAs seeking FDA approval to launch generic sacubitril/valsartan products. (*See, e.g.*, *id.* ¶¶ 9, 19, 31, 64, 73). This case is one of several patent infringement actions filed by Novartis against these generic drugmakers based on Entresto®-related patents. (*See* MDL No. 20-2930-RGA).

On October 24, 2022, Novartis filed a complaint alleging infringement of U.S. Patent No. 11,096,918 (the "'918 patent") by MSN and several other defendants. (D.I. 1). The '918 patent covers the amorphous solid form of a compound ("TVS") present in Entresto® that is comprised of sacubitril, valsartan, and sodium cations. The patent expires on November 8, 2026. (D.I. 1 ¶ 120). Claim 1 of the '918 patent recites:

> 1. An amorphous solid form of a compound comprising anionic [valsartan[3]], anionic [sacubitril[4]], and sodium cations in a 1:1:3 molar ratio.

('918 patent, 32:42–46). Following a Markman hearing, I construed "an amorphous solid form of a compound" to mean "a solid form of a compound in which the amorphous form of the compound predominates. An amorphous solid form is mutually exclusive from a crystalline solid form, but not necessarily mutually exclusive from a partially crystalline solid form." (D.I. 194 at 5).[5]

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[3] The chemical name "(S)-N-valeryl-N-{[2'-(1H-tetrazole-5-yl)-biphenyl-4-yl]-methyl}-valine" recited in claim 1 describes valsartan.

[4] The chemical name "(2R,4S)-5-biphenyl-4-yl-4-(3-carboxy-propionylamino)-2-methyl-pentanoic acid ethyl ester" recited in claim 1 describes sacubitril.

[5] Neither side contests the claim construction for the purposes of this motion. (Hearing Tr. at 24:15–25:12, 50:3–10, 66:8–12).

On July 24, 2024, MSN received final FDA approval for its ANDA product. (D.I. 210 at 1; D.I. 211 at 1). Novartis moves for a preliminary injunction to prevent the prospective at-risk launch of MSN's generic sacubitril/valsartan product. (D.I. 213). Should its motion be denied, Novartis moves for a short stay to allow Novartis to seek injunctive relief from the Federal Circuit. (*Id.*). MSN also moves to strike (D.I. 237) portions of Dr. Matzer's declaration (D.I. 221), which was submitted by Novartis in support of its motion for preliminary injunction.[6]

II. LEGAL STANDARD

"The decision whether to enter a preliminary injunction is committed to the sound discretion of the trial court." *Duraco Prods., Inc. v. Joy Plastic Enters., Ltd.*, 40 F.3d 1431, 1437 (3d Cir. 1994) (quoting *Merchant & Evans, Inc. v. Roosevelt Bldg. Prods. Co.*, 963 F.2d 628, 633 (3d Cir. 1992)). The Third Circuit has cautioned that a preliminary injunction is "an extraordinary remedy" to be granted "only in limited circumstances." *Novartis Consumer Health, Inc. v. Johnson & Johnson-Merck Consumer Pharm. Co.*, 290 F.3d 578, 586 (3d Cir. 2002) (quoting *Instant Air Freight Co. v. C.F. Air Freight, Inc.*, 882 F.2d 797, 800 (3d Cir. 1989)). When seeking a preliminary injunction, a movant "must establish [1] that he is likely to succeed on the merits, [2] that he is likely to suffer irreparable harm in the absence of preliminary relief, [3] that the balance of equities tips in his favor, and [4] that an injunction is in the public interest." *Winter v. Nat. Res. Def. Council, Inc.*, 555 U.S. 7, 20 (2008). The movant must establish the first two requirements before a court considers, to the extent relevant, the remaining two prongs of the standard. *Cipla Ltd. v. Amgen Inc.*, 778 F. App'x 135, 138 (3d Cir. 2019).

[6] Due to the accelerated timeline, Novartis did not have the opportunity to file a response to MSN's motion to strike. Both parties addressed the motion during oral argument. (*See* Hearing Tr. at 3:22–16:12).

III. DISCUSSION

A. Likelihood of Success on the Merits

Novartis argues it is likely to succeed in showing that claim 1 of the '918 patent is valid and infringed by MSN's ANDA product. (D.I. 214 at 3–14). MSN challenges Novartis's likelihood of success of proving infringement, but MSN does not raise any arguments regarding validity. (*See* D.I. 227 at 2–17).

Novartis asserts that testing performed by its expert, Dr. Matzger, revealed that the drug substance in MSN's product contains a small amount of amorphous TVS and does not contain crystalline TVS.[7] (D.I. 214 at 6). Novartis contends the drug substance in MSN's ANDA product, which MSN claims is a crystalline TVS complex and which the parties refer to as "Form-S," is actually a physical mixture of separate crystalline valsartan disodium and separate crystalline sacubitril sodium. (*Id.*). Novartis argues that the amorphous TVS compound therefore necessarily predominates over the (non-existent) crystalline TVS compound. (*Id.*).

MSN argues that Novartis has not shown it is likely to succeed in proving MSN's product contains amorphous TVS. (D.I. 227 at 4–6, 10–15). Novartis's identification of amorphous TVS within MSN's ANDA product relies on Dr. Matzger's Raman mapping data. (D.I. 214 at 4–5). MSN notes that Dr. Matzger did not compare the spectra he obtained from MSN's API to Form-S reference spectra. (D.I. 227 at 10). MSN and its expert, Dr. Steed, argue that Dr. Matzger's test results were therefore based on incomplete data. (D.I. 227 at 10; D.I. 232 ¶¶ 136–37, 141–49; Hearing Tr. at 66:13–73:6). MSN asserts that, when the comparison is made

[7] As I stated during oral argument, I am doubtful of MSN's contention that Dr. Matzger's declaration presented a new infringement theory as opposed to responding to arguments made by MSN's expert. (Hearing Tr. at 8:16–14:25). If I needed to rule on it, I would deny it. I nevertheless do not think I need to rule on it as I find Novartis fails to meet its burden even after full consideration of Dr. Matzger's declaration. Thus, I will dismiss the motion to strike as moot.

between MSN's API spectra and the Form-S reference spectra, the peaks in MSN's API spectra that Dr. Matzger points to as proving the presence of amorphous TVS more closely match the peaks in MSN's Form-S reference spectra than those in amorphous reference spectra. (D.I. 227 at 10; D.I. 232 ¶¶ 136–37, 141–49; Hearing Tr. at 66:13–73:6). Novartis argues the criticism that Dr. Matzger did not use Form-S reference spectra is misplaced because Form-S is not in fact a crystalline TVS complex but a physical mixture of individual crystalline valsartan disodium and individual crystalline sacubitril sodium. (Hearing Tr. at 41:14–42:2). Even if I accept Novartis's assertion as true, however, Dr. Steed's declaration still undermines Dr. Matzger's conclusions by supporting MSN's position that the amorphous regions Dr. Matzger identified are not actually amorphous TVS. I find that Novartis has not met its burden of showing it is likely to succeed in proving MSN's ANDA products contain amorphous TVS.

Furthermore, I find Novartis has not shown it is likely to succeed in proving that Form-S is a physical mixture rather than a crystalline complex. MSN argues that XRPD, Raman, FT-IR, and DSC testing data submitted with its ANDA demonstrates that Form-S is not a physical mixture or amorphous. (D.I. 227 at 3–6, 16–17; D.I. 232 ¶¶ 98, 102, 104–05, 109–12, 175–78, 185–90; Hearing Tr. at 56:5–59:17, 81:16–84:19). Novartis challenges the ANDA testing as flawed because MSN never compared Form-S data to physical mixture data. (Hearing Tr. at 44:10–45:5, 47:18–25, 88:10–25; D.I. 221 ¶¶ 33–34, 50–52). Novartis also contends that MSN's Raman data proves Form-S is a physical mixture. In particular, Novartis argues there are variations between the Raman spectra of the two samples of Form-S that would not be present if Form-S was a crystalline complex. (D.I. 221 ¶¶ 98–100; Hearing Tr. at 46:15–17). Novartis cites Dr. Matzger's Raman data in support of its position that Form-S was a physical mixture. (D.I. 214 at 4–5; D.I. 221 ¶¶ 60–68; Hearing Tr. at 28:17–36:1). MSN argues that Dr. Matzger's

Raman mapping does not show that MSN's API is a physical mixture or amorphous TVS, noting that MSN's Raman spectra from the two samples of Form-S contained different peaks from those that Dr. Matzger relies on to characterize the drug substance. (D.I. 227 at 16; D.I. 232 ¶¶ 180–187; Hearing Tr. at 81:16–13). In the face of supporting test data and what appear to be valid criticisms of said test data from both sides, I am unable to find that the record favors finding Form-S to be one of a physical mixture or a crystalline complex. Novartis bears the burden of proof, both on infringement and on showing likelihood of success. I find it has not met the burden it bears at this stage with regards to demonstrating that Form-S is a physical mixture.[8]

For the reasons above, I conclude Novartis has not shown it is likely to succeed on the merits of showing infringement.

B. Irreparable Harm

Novartis contends it will suffer irreparable harm absent an injunction. (D.I. 214 at 14–18). As an initial matter, I am skeptical about Novartis's characterization of many of its potential harms. For example, Novartis maintains "[a]n at-risk launch by MSN . . . is also likely to trigger at-risk launches by several other generic drugmakers, thereby destroying Entresto®'s market momentum and causing Novartis to suffer immediate irreparable harm in the form of lost sales, lost market share, loss of formulary position, and price erosion." (*Id.* at 15). I do not find it reasonable to attribute harm resulting from the actions taken by other generic drug makers to

[8] In its answering brief, MSN argued Novartis would be unable to show infringement even if the drug substance in MSN's product were proven to be a physical mixture. (D.I. 227 at 17). MSN argued Novartis's infringement theory contradicts my explanation that "construing the term ['amorphous solid form of a compound'] does . . . require looking at looking at the overall makeup of the components within the 'mixture.'" (*Id.*). As MSN did not raise this contention at oral argument and I have ruled in MSN's favor on other grounds, I take no stance on this issue.

MSN's decision to launch its own individual product.[9] Nor do I think it fair to attribute to MSN the harm of impaired promotion of Novartis's other cardiovascular drugs, which would result from Novartis's own profit-maximizing business decision to decrease its cardiovascular product salesforce in response to MSN's launch. (*See id.* at 17–18).

In any event, I believe Novartis has not shown its asserted harms cannot be remedied through monetary damages. *See Automated Merch. Sys., Inc. v. Crane Co.*, 357 F. App'x 297, 301 (Fed. Cir. 2009) ("The burden is . . . on the patentee to demonstrate that its potential losses cannot be compensated by monetary damages."). Novartis and its expert, Dr. Vellturo, offer two main arguments in support of a finding of irreparability, neither of which I find sufficient.

Novartis argues that the "full extent of [its] losses will be difficult—if not impossible—to calculate." (D.I. 214 at 17). Novartis argues that estimating damages would be difficult due to the "complicated and changing dynamics of the heart failure drug market," "uncertainty over how payers will respond to the entry and subsequent withdrawal of generic products," and the "importance of physician and patient education to Entresto®'s continued market momentum." (*Id.* (citing D.I. 219 at ¶¶ 58–62)). The section of Dr. Vellturo's report that Novartis cites in support of this proposition, however, does not discuss these factors.[10] I am unable to find that

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[9] It also seems perverse to allow Novartis to establish irreparability on this basis. Novartis has entered into settlement agreements with multiple generic drugmakers, which I suspect, based on my experience in dealing with such cases, allow all generics to launch if one generic is able to launch. Such a ruling would effectively allow Novartis to maintain its monopoly by the way it has structured its settlements with other companies that threaten its monopoly.

[10] This section of Dr. Vellturo's report focuses on arguing that, because Novartis's internal predictions continually under-forecasted Entresto®'s annual net sales, any lost profits calculations based on these forecasted sales would also understate lost profits. (*See* D.I. 219 at ¶¶ 58–62). Novartis does not emphasize this argument in its briefing and, in any event, Dr. Vellturo has not convinced me that damages would be impossible to calculate. As Dr. McDuff notes, the parties would have the benefit of actual sales and market data on which to base or adjust their damages models. (*See* D.I. 229 ¶ 19). Furthermore, I agree with Dr. McDuff,

Novartis satisfied its burden of establishing that the identified factors (even if I assume their existence) would cause significant difficulty in calculating damages. I agree with the opinion of Dr. McDuff, MSN's expert, that "all of these alleged losses are standard economic analyses that can be quantified and compensated" and that "there are no factors here that make a damages determination particularly unusual or difficult." (D.I. 229 ¶¶ 13–19; *see also Horizon Medicines, LLC v. Alkem Lab'ys, Ltd.*, 2021 WL 10874872, at *1 (D. Del. Aug. 23, 2021) ("Financial harm from launch is complicated, but that is generally true of damages issues in patent cases.")).

Novartis and Dr. Vellturo contend that the monetary damages would likely be beyond MSN's ability to pay. (D.I. 214 at 8–9; D.I. 219 ¶¶ 63–67). I find credible Dr. McDuff's opinion that Dr. Vellturo overstates Novartis's potential loss and understates MSN's potential revenue. (*See* D.I. 229 ¶¶ 21–26 (referencing D.I. 219)). I am confident that MSN, a large generic drugmaker with prior experience in conducting at-risk launches (*see, e.g.*, D.I. 231 ¶ 5 (declaration from an Executive Director of MSN noting two recent at-risk launches conducted by MSN)), would be sufficiently prepared to launch its generic sacubitril/valsartan products without being driven to financial ruin by possible litigation losses. (*See id.* ¶ 11("MSN's current financial condition would allow it to cover the difference between escrowed sales and Novartis' lost profits based on available cash and reserves, and anticipated profits from sales of other products."); *id.* ¶ 12 ("MSN also has the ability to control and limit the amount/volume of

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MSN's expert, that the data suggests that the actual sales tend to track the forecasted sales within some reasonable margin of error and that growth appears to follow a relatively stable trend. (*Id.* ¶ 18 (referencing D.I. 219, Fig. 2, at 27)). I am convinced that the parties' damages experts, to the extent that they would base their calculations on Novartis's internal reports, could make appropriate estimates and adjustments to their models to account for these documented understatements. While there would be some uncertainty inherent in these calculations, "all [damages] approximations involve some degree of uncertainty." *Summit 6, LLC v. Samsung Elecs. Co.*, 802 F.3d 1283, 1296 (Fed. Cir. 2015).

generic sacubitril-valsartan product it manufactures and distributes in the United States, and thereby mitigate its potential financial exposure."); *id.* ¶ 13 ("MSN has the potential to acquire insurance coverage for the profit differential should the Court award Novartis damages.")).

For the stated reasons, I find Novartis has not established irreparable harm.

C. Balance of Equities and Public Interest

My findings on the likelihood of success and irreparable harm factors call for denial of Novartis's request for injunctive relief. While I need not address the balance of equities and public interest prongs, I note that they do not support granting Novartis a preliminary injunction.

Novartis argues that the balance of hardships favors granting the injunction because MSN would likely be unable to cover all the monetary damages. (D.I. 214 at 18). As stated above, I am skeptical that MSN would be unable to compensate Novartis for its losses. I am further convinced that MSN's potential harm from the loss of its first-mover advantage would outweigh the potential harm to Novartis. I find the balance of equities does not favor enjoining MSN's launch.

Novartis argues that generic entry will cause public harm because Novartis would be forced to reduce its efforts to educate physicians and patients and to reduce its patient support programs for Entresto®. (*Id.* at 18–19). I do not believe that Novartis would be "forced" to take any such actions. Based on the billions in annual net revenues that Novartis has earned, and continues to earn, from Entresto® sales (D.I. 219, Fig. 2, at 27), I doubt that maintaining its current level of investment for these services would cause Novartis to face financial hardship. As stated above, I find it unreasonable to attribute the harm that would result from Novartis's profit-driven actions to MSN's launch. I also agree with MSN that the possible decrease in public awareness is likely outweighed by the increased accessibility and affordability of

sacubitril/valsartan drugs that would result from generic competition. (*See* D.I. 227 at 12–13). I find the public interest factor favors denying injunctive relief.

D. 34 U.S.C. § 271(e)(4)(A)

Novartis additionally seeks injunctive relief under 34 U.S.C. § 271(e)(4)(A). (D.I. 214 at 19). Section 271(e)(4)(A) states, "For an act of infringement . . . the court shall order the effective date of any approval of the drug or veterinary biological product involved in the infringement to be a date which is not earlier than the date of the expiration of the patent which has been infringed." No finding of infringement has yet been made. Novartis does not identify any cases indicating § 271(e)(4)(A) provides a basis for a district court to grant a preliminary injunction. Nor do I think the statute provides such authority. As stated above, I also do not find Novartis is likely to succeed in proving infringement. I decline to grant injunctive relief under § 271(e)(4)(A).

IV. CONCLUSION

For the reasons above, Novartis's motion for preliminary injunction (D.I. 213) is **DENIED.**

MSN's motion to strike (D.I. 237) is **DISMISSED AS MOOT**.

I will grant Novartis's request for a stay (*id.*) to allow Novartis to seek injunctive relief from the Federal Circuit. I expect Novartis to appeal this Memorandum Order by filing a notice of appeal today. I further expect Novartis to file emergency motions in the Court of Appeals as soon as possible. With that understanding, Novartis and MSN are hereby ordered to maintain the status quo for 72 hours from the issuance of this Memorandum Order. I expect the Court of Appeals is in the best position to decide whether to continue the stay, and, if it does, for how long.

IT IS SO ORDERED.

Entered this 12th day of August, 2024

United States District Judge