IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

NOVARTIS PHARMACEUTICALS CORPORATION, *Plaintiff*, v. XAVIER BECERRA, in his official capacity as SECRETARY FO HEALTH AND HUMAN SERVICES, and ROBERT M. CALIFF, M.D. in his official capacity as COMMISSIONER OF FOOD AND DRUGS, FOOD AND DRUG ADMINISTRATION, *Defendants*, and MSN PHARMACEUTICALS INC. and MSN LABORATORIES PRIVATE LIMITED, *(Proposed) Intervenor-Defendants*.	Case No.: 1:24:cv:02234-DLF

INTERVENOR-DEFENDANTS' MEMORANDUM IN OPPOSITION TO PLAINTIFF'S MOTION FOR TEMPORARY RESTRAINING ORDER AND/OR PRELIMINARY INJUNCTION

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I. INTRODUCTION

Having failed to obtain a favorable court ruling on its patents that would block MSN Pharmaceuticals Inc., the U.S. regulatory agent for MSN Laboratories Private Limited (collectively, "MSN"), from bringing its generic sacubitril/valsartan tablets to market, Novartis Pharmaceuticals Corporation ("Novartis") seeks the extraordinary remedy of a temporary restraining order or preliminary injunction (collectively, "TRO" or "TRO Motion") to undo MSN's FDA approval as a last-ditch effort to extend its monopoly over the billion-dollar Entresto product. In doing so, Novartis attempts to contort the governing statute and regulations in such a way as to prevent FDA from doing what it has always done – allow generic manufacturers to remove indications from their labels that brand companies contend are covered by certain patents. Not only do the statute and regulations fully support FDA's decision with respect to MSN's Abbreviated New Drug Application ("ANDA"), but any other result would be contrary to Congressional intent in adopting "skinny labeling" as part of the Hatch-Waxman regime to promote generic drug competition and reduce overall drug prices.

Not only does Novartis fail to meet the heavy burden of establishing a likelihood of success on the merits, but it also fails to establish irreparable harm. Novartis hinges its irreparable harm argument on conjecture about the dollars it might lose if a generic product enters the market and challenges its monopoly on its multi-billion dollar product. But, Novartis fails to consider that the revenue decrease is only a small fraction of the company's total worldwide revenue, particularly considering that the time period of sales by MSN would be a matter of mere weeks if this Court were to deny the TRO and consider the issues on an expedited preliminary injunction or summary judgment schedule that would have the benefit of FDA's administrative record and the parties' full briefing addressing such record. Moreover, Novartis fully fails to account for the harm to MSN

that will result from a delay in market entry, nor the public interest in obtaining access to a less expensive generic version of Entresto. When such factors are properly considered and balanced, the Court should deny Novartis' TRO Motion.

II. FACTUAL BACKGROUND

Because the Court is being asked to digest a substantial amount of information on an emergency basis, Intervenor-Defendants offer the following brief summary of the relevant facts:

- Novartis' NDA No. 207620 for Entresto (sacubitril/valsartan) tablets, 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg, was approved by FDA on July 7, 2015. Dkt. No. 1, Ex. H at 14.[1]

- Since that time, Novartis has been marketing Entresto (sacubitril/valsartan) without any generic competition, generating over $10.5 billion in revenue in the U.S. alone based on its monopoly pricing. *See* Dkt. No. 1 at 26.

- As relevant to this case, Entresto's approved labeling contains language directed to specific patient populations with respect to both (i) the approved indication and (ii) dosing information. Dkt. No. 3-1 at 5-10.

- With respect to the approved indication, Entresto was initially approved in July 2015 to treat patients with heart failure and reduced ejection fraction (HFrEF). *Id.* at 6.

- In February 2021, FDA approved a supplement to Entresto's NDA, expanding the indication to additionally include patients with heart failure that did not have reduced ejection fraction (i.e. heart failure with preserved ejection fraction, or HFpEF). *Id.*

- With respect to the dosing information, Entresto's labeling contains information regarding a clinical study referred to as "TITRATION," which tested a modified dosing regimen applicable to patients who had not previously used angiotensin-converting enzyme inhibitors ("ACEis") or angiotensin receptor blockers ("ARBs"). *Id.* at 8-9.

- Novartis owns patents that it asserts cover (i) methods of using sacubitril/valsartan to treat HFpEF patients (U.S. Patent Nos. 9,517,226, 9,937,143, and 11,135,192),

[1] Documents referenced by their docket entry are cited to the pagination in the document itself, rather than by the pagination assigned by the docket.

and (ii) the modified dosing regimen reflected in the TITRATION study (U.S. Patent No. 11,058,667). *Id*. at 15.

- In September 2022, Novartis submitted a citizen petition to FDA requesting that FDA refrain from approving ANDAs that "carve out" labeling language related to either: (i) treatment of HFpEF patients, or (ii) the modified dosing protocol reflected in the TITRATION study. Novartis argued that, *inter alia*, such carveouts violate FDA's regulations and would present safety and efficacy risks. Accordingly, Novartis requested that FDA refrain from approving any ANDA referencing Entresto and containing such labeling alterations. *Id*. at 10-11.

- FDA denied Novartis' petition on July 24, 2024, in an exhaustive 45-page letter detailing the reasons why the labeling alterations in question were proper under the relevant statute and regulations and would not make the related products any less safe or effective. *See* Dkt. No. 1, Ex. H.

- On the same day, FDA approved MSN's ANDA No. 213748 for a generic version of Entresto,[2] demonstrating that MSN's sacubitril/valsartan ANDA met the scientific and technical requirements for approval. Dkt. No. 3-1 at 11.

III. LEGAL STANDARD

A temporary restraining order is an "extraordinary and drastic" remedy that "may only be awarded upon a clear showing that the plaintiff is entitled to such relief" *Winter v. Nat. Res. Def. Council, Inc.*, 129 S. Ct. 365, 376 (2008); *see also Mpoy v. Fenty*, 674 F. Supp. 2d 163, 165 (D.D.C. 2009) ("Injunctive relief is an extraordinary remedy, and plaintiff bears a substantial burden to obtain it."); *Hall v. Johnson*, 599 F. Supp. 2d 1, 6 n.2 (D.D.C. 2009) ("The same standard applies to both temporary restraining orders and to preliminary injunctions."). To obtain such extraordinary relief, Novartis must establish that: (1) it is likely to succeed on the merits; (2) it is likely to suffer irreparable harm in the absence of preliminary relief; (3) the balance of equities

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[2] Information on MSN's approval is available at: https://www.accessdata.fda.gov/scripts/cder/ob/results_product.cfm?Appl_Type=A&Appl_No=213748#167.

tips in its favor; and (4) an injunction would serve the public interest. *Winter*, 129 S. Ct. at 374.

It is "particularly important" for a movant to demonstrate likely success on the merits. *Astellas Pharma US, Inc. v. FDA*, 642 F. Supp. 2d 10, 16 (D.D.C. 2009). "[A]bsent a substantial indication of likely success on the merits, there would be no justification for the court's intrusion into the ordinary processes of administration and judicial review." *Id.* Moreover, a party seeking preliminary injunctive relief must demonstrate an actual "likelihood" of success on the merits, not merely the existence of "questions so serious, substantial, difficult and doubtful, as to make them fair ground for litigation . . . ." *Munaf v. Geren*, 553 U.S. 674, 690 (2008) (internal quotation marks and citations omitted). Nor is a mere "possibility" of irreparable harm sufficient to justify such relief. An "irreparable injury" must be "likely in the absence of an injunction," for "[i]ssuing a preliminary injunction based only on a possibility of irreparable harm is inconsistent with our characterization of injunctive relief as an extraordinary remedy that may only be awarded upon a clear showing that the plaintiff is entitled to such relief." *Winter*, 129 S. Ct. at 375-76 (citations omitted, emphasis in original).

IV. ARGUMENT

A. Novartis is not likely to succeed on the merits.

1. FDA has broad authority to approve generic drug labels that carve out protected indications.

FDA's approval of MSN's carved-out indication was well within the authority granted by statute and consistent with FDA's regulations, prior practice, and case law. In fact, allowing generic companies to carve out indications and other protected language from their labels in order to navigate patents or regulatory exclusivities is a long-established practice consistent with the Congressional purpose behind the Hatch-Waxman Act "to get generic drugs into the hands of patients at reasonable prices – fast." *In re Barr Labs, Inc.*, 930 F.2d. 72, 76 (D.C. Cir. 1991).

Starting with the statute, although generic drug labels typically match the labeling of their branded counterpart, Congress expressly authorized exceptions where "the new [ANDA] drug and the listed [brand] drug are produced and distributed by different manufacturers." 21 U.S.C. § 355(j)(2)(A)(v). One of the driving reasons for this allowance was Congress's desire to promote generic competition by "permit[ing] an ANDA [for a generic drug] to be approved for less than all of the indications for which the [branded] listed drug has been approved . . . [T]he applicant need not seek approval for all the indications for which the listed drug has been approved." House Report No. 98-857, pt 1, at 21 (1984). Congress thus designed the "same labeling" statutory requirements to allow label changes for products produced by generic companies that are different from the branded company and further specified that the generic manufacturers can avoid the related Hatch-Waxman patent litigation by submitting section viii statements under 21 U.S.C. § 355(j)(2)(A)(viii) instead of a Paragraph IV certification under 21 U.S.C. §355(j)(2)(A)(iv), which would otherwise lead to patent litigation and delay the approval of the ANDA. The use of so-called "skinny" labeling has become a driving force in promoting generic competition and lowering drug costs. *See Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405, 132 S.Ct. 1670, 182 L.Ed.2d 678 (2012) (noting that the Hatch-Waxman Act's skinny-label provisions were enacted to "speed the introduction of low-cost generic drugs to market"); *Takeda Pharms. USA, Inc. v. W.-Ward Pharm. Corp.*, 785 F.3d 625, 631-32 (Fed. Cir. 2015) (holding that a central purpose of the Hatch-Waxman Act is to allow through the section viii carve out process, the sale of generic drugs for unpatented uses); Ex. A, Engilman, et. al., *Estimated Medicare Part D Savings From Generic Drugs With a Skinny Label*, Annals of Internal Medicine, Vol.177:6 (April 30, (2024) (finding that competition from skinny label generics saved Medicare Part D nearly $15 billion from 2015 to 2021).

Novartis improperly attempts to narrow the statutory language by arguing that the "different manufacturer" statutory language only allows for changes relating to identifying "a different manufacturer, product name, or company address." Dkt. No. 3-1 at 19. But Novartis can point to no statutory language that is so narrowly restrictive, and such a construction would nullify the submission of section viii statements under 21 U.S.C. § 355(j)(2)(A)(viii). It is a cardinal rule of statutory construction, however, that statutes should be construed as a whole and that a court should not construe one statutory provision in such a way as to nullify another statutory provision. *Trustees of IAM Nat'l Pension Fund v. Ohio Magnetics, Inc.*, 656 F. Supp. 3d 112, 136 (D.D.C. 2023), aff'd sub nom. *Trustees of IAM Nat'l Pension Fund v. M & K Emp. Sols.*, LLC, 92 F.4th 316 (D.C. Cir. 2024) (holding that to the extent possible, courts must avoid reading one provision of a statute to nullify the significance of another). Yet, Novartis's construction of the "same labeling" statutory requirement would entirely render meaningless the section viii statutory provisions because it would not allow generic companies to carve any language from the brand label in order to avoid brand company patents.

Perhaps realizing that its statutory argument is not sufficient to nullify FDA's longstanding regulations, Novartis next argues that FDA's approval of MSN's skinny label violates FDA's own regulations. Dkt. No. 3-1 at 18-19. But again, Novartis's interpretation of the regulations is too narrow and misconstrues the changes that FDA allowed MSN to make in its label. Specifically, FDA's regulations permit labeling changes based on "the omission of an *indication or other aspect* of labeling protected by the patent or accorded exclusivity under the [the FDCA]." 21 C.F.R. § 314.94(a)(8)(iv) (emphasis added). Additionally, the regulations set forth specific *examples* of permissible differences in labeling that may result because the generic drug product and listed drug product are produced by different manufacturers. These include "differences in expiration date,

formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of indication *or other aspect of labeling* protected by patent or accorded exclusivity under [the FDCA]." 21 C.F.R. § 314.94(a)(8)(iv). Importantly, the regulation does not recite an exclusive list of labeling differences that FDA may approve, but it lists examples of what the "differences between [ANDA] labeling and labeling approved for the reference listed drug *may include*." 21 C.F.R. § 314.94(a)(8)(iv) (emphasis added).

Here, FDA's approval of MSN's label changes are precisely the kind envisioned by the regulations. MSN's label carves out Novartis's indication to treat a subset of patients that do not have reduced ejection fraction (i.e. HFpEF patients). However, the only feasible way for MSN to omit the protected language is by making minor attendant changes to the label. Under the current approved label for Entresto, Novartis's purportedly patent-protected indication (i.e. treatment of HFpEF patients) is incorporated into a generally-stated broader indication that also incorporates non-patent protected indications (i.e., treatment of patients with reduced ejection fraction). Specifically, the Entresto label states that the product is indicated "to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients **with chronic heart failure."** Dkt. No. 1, Ex. A (emphasis added). "Patients with chronic heart failure" encompasses both the treatment of patients that are within the purportedly patent-protected indication (i.e., HFpEF patients) as well those that are not (i.e., HFrEF patients). Therefore, MSN's label modifies the indication as follows: "to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure~~.~~ **and reduced ejection fraction**. ~~Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal.~~" ANDA No. 213748. The bolded text is language that MSN was required to add to clarify that its

ANDA product is not indicated for treating HFpEF patients but is instead limited to treating patients with HFrEF (i.e., reduced ejection fraction). The insert is a *de minimis* change for the sole purpose of carving out an indication that Novartis asserts is protected by its patents, which is expressly permitted by the section viii provisions under 21 U.S.C. § 355(j)(2)(A)(viii).

To prohibit this modification would create a precedent where any brand manufacturer could circumvent section viii statements entirely by carefully wording its indications. For example, instead of drafting a label to treat Pox A, Pox B, and Pox C (where Pox C is still protected under a patent), a manufacturer could draft an indication for "all Pox variants." Under Novartis's theory, a generic manufacturer would be prohibited from submitting an indication for "all Pox variants, **except for Pox C**" or for "Pox A and Pox B" because it would require "adding" words or phrases to the label. Such an absurd result that is clearly contrary to Congressional intent should not be countenanced by the Court. *Griffin v. Oceanic Contractors, Inc.*, 458 U.S. 564, 575, 102 S. Ct. 3245, 3252, 73 L. Ed. 2d 973 (1982) (recognizing that interpretations of a statute which would produce absurd results are to be avoided if alternative interpretations consistent with the legislative purpose are available).

Relevant case law affirms FDA's authority to approve a generic drug manufacturer's carved out label without violating the same labeling requirement. For example, in *Bristol-Myers Squibb Co. v. Shalala*, the DC Circuit affirmed FDA's authority to approve indication carve outs, holding that "the statute expresses the legislature's concern that a drug be safe and effective for each indication that will appear on its label; whether the label for the new generic lists every indication approved for use of the pioneer is a matter of indifference." 91 F.3d. 1493, 1500 (D.C. Cir. 1996). Similarly, in *Sigma-Tau Pharmaceuticals, Inc. v. Schwetz*, the Fourth Circuit upheld the right of an ANDA applicant to remove an indication protected by orphan drug exclusivity. 288

F.3d. 141 (4th Cir. 2002). The court observed that the orphan drug exclusivity was disease specific and not drug specific and reasoned that "[Sigma-Tau's theory] to bar the approval or generic drugs, even for unprotected indications . . . [would add] a huge evidentiary hurdle to the generic drug approval process [and] would be profoundly anti-competitive." *Id.* at 147. Similarly, Novartis is attempting to extend its monopoly beyond what is permitted by law.

Novartis inaccurately summarizes the applicable statute, regulations, and case law in its assertion that labeling differences must take the form of "an ***omission*** of language, not the ***addition*** of language to the current labeling." Dkt. No. 3-1 at 4. But, neither the statute nor regulations prohibit the addition of words or phrases as a method for removing an indication protected by a patent. To do so would conflict with Congress's intent to allow generic manufacturers to seek approval for a drug with fewer indications than the listed drug. If the Court accepts Novartis's assertion, the company would be permitted to extend its monopoly solely because the only way to omit its protected indication is by adding words to the labeling. Neither the text nor the spirit of the law is so restrictive.

As noted in FDA's response to Novartis's Citizen Petition, the agency has permitted the omission of an indication via a carveout where the only way to omit the protected indication was to add words. *See* Dkt. No. 1, Ex. H at 36. For example, in a matter involving facts that are nearly identical to the facts at issue here, for the drug Velcade (bortezomib), FDA allowed a "carve-in" with an older version of an indication with added language that limited the patient population to second-line lymphoma patients. Due to the way the labeling was written, the only way to omit the protected indication was to add words to the labeling to specify the more limited patient population. Specifically, the labeling was modified as follows: "for the treatment of patients with mantle cell lymphoma **who have at received at least 1 prior therapy**." The bolded language represents the

added language departing from the branded indication. FDA found this approach to be consistent with the agency's past practice as well as with the scope of Velcade's exclusivity. FDA Docket No. FDA-2017-P-3672, FDA response to Citizen Petition Regarding Velcade (bortezomib) (November 6, 2017) at 14 *available at* https://www.regulations.gov/document/FDA-2017-P-3672-0022. It was thus proper for FDA to do the same with respect to MSN's ANDA here in order for FDA to meet the requirement that an agency treat like situations alike. *Westar Energy, Inc. v. Fed. Energy Regul. Comm'n*, 473 F.3d 1239, 1241 (D.C. Cir. 2007) ("a fundamental norm of administrative procedure requires an agency to treat like cases alike"). Any other decision by FDA would have been arbitrary and capricious.

Novartis's argument that FDA approved MSN's label based on "discontinued labeling" is a red herring. Dkt. No. 3-1 at 10. MSN's label relied on Novartis's current label and carved out the protected indication (i.e., the HFpEF patient population) from the currently approved label. It just so happens that this carve-out matches language from a prior version of the label before Novartis obtained approval to treat this additional patient population. This was also the situation with Velcade, where FDA found it appropriate to omit the exclusivity-protected indication, such that the generic indication matched a previous iteration of the branded label. *See* Dkt. No. 1, Ex. H at 36. FDA's decision to approve MSN's ANDA label was thus well within the statutory and regulatory provisions, along with being consistent with FDA's prior determinations and Congressional purpose in lowering drug prices by allowing skinny labels. Novartis's TRO motion should therefore be denied.

2. FDA's factual determinations as to drug safety and efficacy enjoy high levels of respect and are typically undisturbed by the courts.

Novartis argues that FDA's approval of the carve out of the TITRATION study information was unlawful because removal of this "critical safety information" renders MSN's drug product

less safe and effective in contravention of 21 C.F.R. § 314.127(a)(7). Dkt. No. 3-1 at 21. However, the characterization of the carved-out TITRATION data as "critical safety information" is merely a blanket conclusion by Novartis, unsupported by expert opinion or scientific analysis. In making this argument, Novartis seeks to have this Court second-guess FDA's scientific judgment regarding drug safety and efficacy. Courts, however, consistently decline to engage in this type of back-seat driving,[3] and Novartis has not demonstrated a sufficient reason to depart from this norm.

Courts recognize that FDA's determination of safety and efficacy is a highly factual inquiry, demanding a rigorous scientific evaluation and the experience and expertise to make that possible. *Weinberger*, 412 U.S. at 653-54 ("The determination whether a drug is generally recognized as safe and effective . . . necessarily implicates complex chemical and pharmacological considerations.") Accordingly, courts have recognized that FDA, with its staff of more than 12,000 scientists[4], is best suited to undertake this analysis. *Pharm. Mfg. Research Servs.*, 957 F.3d at 262 ("In the context of a challenge to the FDA's decision making, the court gives a high level of deference to the agency's scientific analysis of the evidence before it, and must avoid unduly second-guessing those scientific judgments."); *Premo Pharmaceutical Laboratories*, 629 F.2d at 803 ("The entire statutory scheme envisages that the FDA will perform the difficult task of investigation and scientific evaluation usually required to determine whether a drug product is safe and effective.")

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[3] *See, e.g.*, *Weinberger v. Bentex Pharmaceuticals, Inc.*, 412 U.S. 645, 654 (1973); *Pharm. Mfg. Research Servs. v. FDA*, 957 F.3d 254, 262 (D.C. Cir. 2020); *Cytori Therapeutics, Inc. v. Food & Drug Admin.*, 715 F.3d 922, 927 (D.C. Cir. 2013); *Premo Pharmaceutical Laboratories, inc. v. United States*, 629 F.2d 795, 803 (2nd Cir 1980).

[4] *See* U.S. Food and Drug Administration, FDA STEM Outreach, Education and Engagement, https://www.fda.gov/science-research/fda-stem-outreach-education-and-engagement#:~:text=More%20than%2012%2C000%20of%20FDA's,statisticians%2C%20veterinarians%2C%20and%20engineers.

Findings of fact made by agencies within their area of expertise are afforded great weight and respect and are typically left undisturbed by courts. *Weinberger*, 412 U.S. at 653-54 ("Threshold questions within the peculiar expertise of an administrative agency are appropriately routed to the agency, while the court stays its hand."). The deference afforded these determinations predated *Chevron, U.S.A., Inc. v. Nat. Res. Def. Council, Inc.*, 467 U.S. 837 (1984), and is therefore unaffected by the Supreme Court's recent decision in *Loper Bright Enterprises v. Raimondo*, 144 S. Ct. 2244 (2024). As recognized by Novartis (*see* Dkt. No. 3-1 at 19), *Chevron* and *Loper Bright* grappled with the issue of whether "an agency interpretation of ***law***" is entitled to deference. In contrast, it has never been controversial that an agency's determinations of ***fact*** – especially highly technical facts within an agency's special expertise – are to be treated with serious respect. As the Supreme Court noted in *Loper Bright*, well before the advent of *Chevron* deference, "the Court often treated agency determinations of *fact* as binding on the courts, provided there was 'evidence to support the findings.'" *Loper Bright*, 144 S.Ct. at 2258 (emphasis in original). And, the *Loper Bright* Court noted that "Section 706 [of the Administrative Procedure Act] *does* mandate that judicial review of agency policymaking and factfinding be deferential." *Loper Bright*, 144 S. Ct. at 2261.

Review of factual determinations "focuses on whether the agency's decision was reasonable and reasonably explained, and based on consideration of the relevant factors." *Pharm. Mfg. Research Servs.*, 957 F.3d at 262. The Supreme Court has long recognized that agency judgments on technical issues within their scope of expertise are to be given persuasive weight based on their thoroughness and the validity of the agency's reasoning. *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944).

In evaluating whether MSN's carve out of the TITRATION information was permissible

under 21 C.F.R. § 314.127(a)(7), FDA engaged in a highly reasoned and technical analysis, which is set out in exhaustive detail in its 45-page response to Novartis' Citizen Petition ("Response"). *See* Dkt. No. 1, Ex. H. After over 10 pages of thorough discussion of the underlying scientific principles and data, FDA explains, *inter alia*:

- "The omission of the subsection 2.6 modified dosing regimen from the labeling of generic sacubitril and valsartan tablets would not render these drugs less safe or effective than Entresto for the remaining nonprotected conditions of use because the WARNING AND PRECAUTIONS section (section 5) of labeling are sufficient to mitigate the risk of Entresto's important adverse reactions." *See* Dkt. No. 1, Ex. H at 39 (emphasis added).

- "Whether the section 2.6 dosing modification is the safest and best-tolerated option for such patients, as you contend in the Petition, is unknown because initiation using this dosing regimen has only been studied in an uncontrolled manner (i.e., single-blind run-in from TITRATION)." *See Id*. at 40 (emphasis added).

- "As explained above, TITRATION studied 498 HF patients who were randomized to the modified dose (24/26 mg or E50) or standard dose (49/51 mg or E100) regimen…All patients had to tolerate a single-arm run-in with E50, limiting generalizability to truly naïve patients." *Id*. (emphasis added).

- "Notably, the rates of hypotension, renal dysfunction, and hyperkalemia observed in TITRATION were similar between the two groups. As discussed above, TITRATION was a supportive phase 2 trial and suggested that ACEi- or ARB-naïve/low dose patients might benefit from a slow up-titration regimen with a lower starting dose to increase tolerability and reduce the risk of adverse reactions such as hypotension, hyperkalemia, and renal impairment. Although TITRATION provided some information about the safety profiles of the standard and modified dosing regimens…the results of TITRATION are not robust." *Id*. at 40-41 (emphasis added).

- "Therefore, while TITRATION supports the dosing recommendation in section 2.6 for ACEi- or ARB-naïve/low dose patients, it does not provide a scientific basis to conclude, as you assert in your Petition, that the standard Entresto dosing regimen puts such patients at a greater risk of adverse reactions or that section 2.6 is "critical" to ensuring the safe and effective use of generic sacubitril and valsartan product." *Id*. at 41 (emphasis added).

Accordingly, in asking this Court to adjudicate the accuracy of FDA's analysis and conclusions summarized above, Novartis is asking the Court to, *inter alia*, (i) evaluate the adequacy of certain methodologies for clinical studies, (ii) determine how far scientific data in a

particular patient population may be extended to apply to other patient populations, and (iii) draw scientific conclusions as to medical risk from clinical data. Perhaps even more shocking, Novartis is asking the Court to do that in an emergency TRO proceeding without even having the benefit of FDA's administrative record or full briefing of the parties addressing that record. To the contrary, Novartis does not even offer a full view of FDA's analysis in its memorandum for this Court's consideration. Rather, Novartis presents mere snippets of FDA's reasoning, often divorced from their proper context, while completely ignoring, or even obscuring, the overall conclusions that run contrary to Novartis' arguments. For example, Novartis cites to isolated phrases from FDA's Response to allege that "[w]hile the modified dosing regimen 'might' be beneficial to ACE/ARB naïve patients, the agency asserts that there is no need for such patients to receive the 'safest and best-tolerated option.'" Dkt. No. 3-1 at 29. While FDA's Response does indeed use the quoted phrases, it is in service of a completely different conclusion, which Novartis fails to mention – that while the TITRATION study leaves open the possibility that the modified dosing regimen "might" be beneficial, "[w]hether the section 2.6 dosing modification is the *safest* and *best-tolerated* option for such patients . . . ***is unknown*** because initiation using this dosing regimen has only been studied in an uncontrolled manner . . . ." *See* Dkt. No. 1, Ex. H at 40 (emphasis added).

But, even if FDA's reasoning had been fully presented and the full administrative record was available, such a review of the scientific merits of FDA's determination is beyond the narrow scope of review for prohibited "arbitrary and capricious" behavior. *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto Ins. Co.*, 463 U.S. 29, 43 (1983); *see also Friedman v. FAA*, 890 F.3d 1092, 1098-99 (D.C. Cir. 2018). "Meaningful review of an agency's actions does not require the reviewing court to step into the FDA's shoes and reassess its scientific judgments—a role that courts are ill-equipped to play under the guise of the APA's arbitrary and capricious standard."

Pharm. Mfg. Research Servs., 957 F.3d at 265; *see also Cytori*, 715 F.3d at 927 ("In Administrative Procedure Act cases alleging arbitrary and capricious agency action, courts must be careful not to unduly second-guess an agency's scientific judgments."). Instead, the Court's role is to ensure that FDA has undertaken a thorough, reasoned analysis and reached an evidentiary-based conclusion. FDA has clearly done so here, and Novartis is unlikely to succeed in its attempt to have the Court supersede FDA's highly technical, scientific conclusions. Novartis's TRO motion should thus be denied.

B. Novartis cannot demonstrate irreparable injury from approval and launch of MSN's generic product.

A temporary restraining order is an "extraordinary and drastic" remedy that "may only be awarded upon a clear showing that the plaintiff is entitled to such relief." *Winter v. Nat. Res. Def. Council, Inc.*, 129 S. Ct. 365, 376 (2008); *see also Mpoy v. Fenty*, 674 F. Supp. 2d 163, 165 (D.D.C. 2009) ("Injunctive relief is an extraordinary remedy, and plaintiff bears a substantial burden to obtain it."); *Hall v. Johnson*, 599 F. Supp. 2d 1, 6 n.2 (D.D.C. 2009) ("The same standard applies to both temporary restraining orders and to preliminary injunctions."). The irreparable injury requirement "erects a very high bar for a movant." *Coal. for Common Sense in Gov't Procurement v. United States*, 576 F. Supp. 2d 162, 168 (D.D.C. 2008). The movant must show that the irreparable injury is "neither remote nor speculative, but actual and imminent." *Direx Israel, Ltd. v. Breakthrough Medical Corp.*, 952 F.2d 802, 812 (4th Cir. 1991) (quoting *Tucker Anthony Realty Corp. v. Schlesinger*, 888 F.2d 969, 975 (2d Cir. 1989)). In other words, "[t]he claimed injury must be both certain and great" and "of such *imminence* that there is a clear and present need for equitable relief to prevent irreparable harm." *Beck v. Test Masters Educ. Servs. Inc.*, 994 F. Supp. 2d 98, 101 (D.D.C. 2014) (internal quotation marks and citations omitted)). Novartis fails to meet this heavy burden.

1. Novartis' immense global revenue will not be materially affected by the launch of a generic.

Novartis is a multinational pharmaceutical company with total annual revenue of $47.733 billion from March 31, 2023 to March 31, 2024. *See* Novartis AG Revenue 2010-2024 | NVS. MacroTrends.https://www.macrotrends.net/stocks/charts/NVS/novartis-ag/revenue#google_ vignette; Novartis AG, (18 July 2024). Form 6-K, Exhibit 99.1 Financial Report Q2 2024. Retrieved from SEC EDGAR website https://www.sec.gov/ix?doc=/Archives/edgar/data/ 0001114448/000137036824000019/nvs-20240630.htm. Although Novartis projects that Entresto will experience an extreme loss in sales, including 85-90% market loss in the first three months of generic entry, its predictions constitute an exaggerated plea proffered simply to prolong its monopoly. *See* Dkt. No. 3-2 at ¶¶ 9, 24. Although Novartis publicly reported over $47 billion in global revenue for the year ended March 31, 2024, it attempts to narrowly focus on only its U.S. sales to argue that its $3 billion in U.S. Entresto sales accounts for 17% of its total U.S. sales. *See* Dkt. No. 1 at 12. But, the $3 billion in U.S. sales for Entresto in 2023 constitutes a mere 6.28% of global revenue for the year ended March 31, 2024. Even assuming that Novartis was correct that it would lose 85-90% of Entresto revenue in three months, such a loss (i.e., $3 billion in annual U.S. sales equates to about $250 million per month, so three months constitutes about $750 million in U.S. revenue, and an 85-90% reduction in sales over three months equates to $637.5 to $675 million in lost U.S. revenue) still only constitutes about 5.3-5.7% of global revenue over that same three month period (i.e., $47.733 billion in annual sales equates to about $11.93 billion in total sales over 3 months, and a $637.5 to $675 million decrease in revenue only constitutes about 5.3-5.7% of global sales over this period). Such a small percentage loss of sales certainly cannot constitute irreparable harm. *See Bristol-Myers Squibb Co. v. Shalala,* 923 F. Supp. 212, 220 (economic loss is not "irreparable harm" where (1) the projected lost sales accounted for only a

small percentage of the company's total sales, and (2) the company would "undoubtedly survive as a going business concern . . . [and] its total sales picture will not be greatly affected" by the loss of market share); *see also Mylan Labs, Inc. v. Leavitt,* 484 F. Supp. 2d 109, 123 (D.D.C. 2007); *Biovail Corp. v. FDA*, 448 F. Supp. 2d 154, 164 (D.D.C. 2006) (citing *BMS,* 923 F. Supp. at 221); *Astellas Pharma US, Inc.*, 642 F. Supp. 2d at 21-23 (no irreparable injury even though approval of a generic product would injure plaintiff because the generic product would compete with plaintiff's top selling drug that constituted approximately half of its revenue); *Sandoz, Inc. v. FDA,* 439 F. Supp. 2d 26 (D.D.C. 2006). The fact that FDA is immune from a suit for damages "is immaterial to the court's consideration." *Biovail Corp. v. FDA,* 519 F. Supp. 2d 39, 49 (D.D.C. 2007).

2. Novartis' assertions and methodology for arguing irreparable harm are speculative and based on inaccurate timelines.

Novartis' claims that Entresto would experience "dramatic loss of sales in the weeks and months following generic entry" and industry trends showing that branded products lose between 85-90% of market volume in the first three months after generic launch are unfounded and overstated. *See* Dkt. No. 3-2 at ¶¶ 9, 24; Dkt. No. 3-1 at 26. Specifically, the data cited in the Declaration of Kristin Miller in support of the TRO Motion is based on speculation and "analogs that [Novartis'] market access team monitors" reporting that 80% of market volume is lost in six months following generic entry. *See* Dkt. No. 3-2 at ¶¶ 9, 24.

If the TRO is rightly rejected, however, Novartis will still have the opportunity to pursue, and the Court will have the time and opportunity to adequately assess, a preliminary injunction motion or summary judgment motion with the benefit of FDA's administrative record and full briefing by the parties. Such a process can be scheduled within weeks, not three to six months, so Novartis' projections for losses at three or six months are overstated. At most, MSN is likely to be on the market only for a matter of weeks before the preliminary injunction and/or summary

judgment motion is resolved. Indeed, recent articles have reported generic market penetration closer to 50% at approximately one month, not the 85-90% asserted by Novartis, although Novartis relies on the very same article when asserting that "[i]t is well known in the pharmaceutical industry that generic drugs quickly replace branded products in the marketplace soon after their launch." *See Grabowski et al., Continuing Trends In U.S. Brand-Name And Generic Price Competition*, 24 J. OF MEDICAL ECONOMICS, Fig. 5 (2021); Dkt. No. 3-1 at 12, 26. Utilizing Novartis' reported $3 billion in U.S. sales for Entresto in 2023, Novartis realizes about $250 million in U.S. sales per month. A 50% market penetration in the first month for a generic sacubitril/valsartan tablet product would constitute about $125 million in missed revenue from Novartis, which constitutes a mere ***0.26%*** of Novartis' $47.733 billion total global revenue for the year ended March 31, 2024.

Even Novartis' own financial reporting undercuts its arguments. For example, in its July 18, 2024 6-K, Novartis reported a mere 4% decrease in total sales due to generic entry, across all product lines. Novartis AG, (18 July 2024). *Form* 6-K, Exhibit 99.2 Interim Financial Report. Retrieved from SEC EDGAR website https://www.sec.gov/ix?doc=/Archives/edgar/data/0001114448/000137036824000019/nvs-20240630.htm. Past instances of generic entry for other Novartis products suggest a much smaller initial market penetration. For example, the first generic for Novartis product Gilenya launched on September 22, 2022. *See* Optum Rx, Gilenya (fingolimod) – First-time generic, https://professionals.optumrx.com/content/dam/optum3/professional-optumrx/news/rxnews/new-generics/newgenerics_gilenya_2022-0929.pdf]. In its 6-K reporting on December 31, 2022, Novartis noted that sales of Gilenya decreased 47% year over year for the fourth quarter of 2022 as compared to the fourth quarter of 2021. *See* Novartis AG, (1 February 2023). *Form* 6-K, Exhibit

99.1 Financial Report Q4 2022. Retrieved from SEC EDGAR website https://www.sec.gov/Archives/edgar/data/1114448/000137036823000008/a230201-99_1.htm. A 47% decrease in market share over three months is significantly less than what Novartis is attempting to argue for market erosion (again, 85-90% loss of market volume within three months of generic entry), and this decrease occurred over a *three-month* period as opposed to the matter of weeks that would be the expected timeline for the Court to rule on a preliminary injunction or summary judgment motion. Thus, Novartis overstates its anticipated losses, as the appropriate measure is just the period until the Court can address the full merits in this case. *See Apotex, Inc. v. FDA*, No. 06-0627, 2006 WL 1030151 at *17 (D.D.C. April 19, 2006); *Mylan Pharms. Inc. v. Shalala*, 81 F. Supp. 2d 30, 43 (D.D.C. 2000); *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp., at 221.

3. Novartis' claims of forced personnel cuts are exaggerated and do not reflect the realities acknowledged in Novartis' own motion.

Novartis argues that market erosion from MSN's generic entry will lead to immense personnel cuts. Specifically, Novartis argues that, because revenue from Entresto is a "critical part" of development of new therapies and research, it will be "forced to make difficult personnel decisions that would affect hundreds of Novartis employees . . . [and that it] would be unable to simply redeploy these cardiovascular product-trained representatives." Dkt. No. 3-1 at 29-30. Yet, Novartis simultaneously asserts that it is expanding into the cardiovascular marketplace further, with its FDA-approved drug, LEQVIO. *See* Dkt. No. 3-1 at 29. Novartis does not explain why it would not re-deploy its cardiovascular product-trained representatives to aid in the expansion and development of its other cardiovascular product, LEQVIO. Nor does Novartis explain why it would choose to layoff what it deems to be important personnel for the short period of time it will take for the Court to hear this dispute under an expedited preliminary injunction or summary

judgment schedule that would have the benefit of FDA's administrative record and the parties' fulsome discussion of that record.

4. Novartis has been preparing for generic market entry in the near future.

Even under the best-case scenario, Novartis anticipated loss of exclusivity and generic competition for Entresto by mid-2025. When asked about the timing of potential Entresto generic entry, Novartis' CEO, Vasant Narasimhan, responded that "we can never exclude, of course, somebody trying to do something at risk," and offered an estimate of generic competition in the U.S. by mid-2025. Novartis. *2024 Q2 results presentation and transcript*. Novartis. https://www.novartis.com/investors/financial-data/quarterly-results/2024-q2-transcript#:~:text=Now%20Q2%20sales%20grew%2011,40%25%20up%20in%20US%20dollars; Novartis. 2024 *Q1 results presentation and transcrip*t. Novartis. https://www.novartis.com/investors/financial-data/quarterly-results/2024-q1-transcript]. Given the proximity to Novartis' best-case scenario of generic competition in mid-2025, the potential launch of an Entresto generic competitor, either by MSN or another, in the second half of 2024 is something for which Novartis should be prepared and cannot regard as surprising or irreparable. *See Otsuka Pharm. Co. v. Burwell*, No. GJH-15-852, 2015 WL 1962240, at *11 (D. Md. Apr. 29, 2015) (finding no irreparable harm because Otsuka had been aware of and planned for generic competition for Abilify).

5. Novartis' speculative allegations of reputational harm are routinely rejected by courts.

Novartis further speculates that it will suffer reputational harm and loss of goodwill due to differences between Entresto and MSN's generic with respect to quality and safety. *See* Dkt. No. 3-1 at 28-29. Courts routinely reject such speculative allegations of reputational injury, however, as insufficient to show irreparable harm. For example, this Court rejected the same argument in

Bristol-Myers Squibb Co. v. Shalala, 923 F. Supp., at 220-22, because "[t]here [was] nothing before the court which would lead it to conclude that [the generic drug] will cause any harmful health effects." *See also Astellas Pharma U.S., Inc. v. FDA*, 642 F Supp. 2d 10, 23 (D.D.C. 2009) (rejecting plaintiff's reputation argument because the concerns were "entirely speculative" and lacked evidentiary support). Here, Novartis' allegations of quality or safety issues associated with MSN's product are unfounded.

C. The balance of hardships militates against the extraordinary relief sought by Novartis.

Novartis contends that there will be no irreparable harm to MSN should the Court grant the TRO because TROs effectively maintain the status quo and MSN has yet to launch its product. These assertions fail to appreciate the significant market positioning and revenue impact that would result in irreparable harm to MSN if a TRO is granted and MSN is unable to launch its generic product in the near term.

MSN is one of five "first applicants" that filed Paragraph IV certifications on the same first day. In addition to MSN, it is our understanding that Alembic (ANDA No. 213682), Crystal (ANDA No. 213605), Zydus (ANDA No. 213719), and Laurus (ANDA No. 213676) are also first applicants. *See* https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=207620. Although, these other applicants have obtained final approval of their ANDAs without following the labelling approach adopted by MSN and approved by FDA, each of them have instead entered into settlement agreements with Novartis, presumably preventing them from launching their respective generics at this time. *See* Crystal consent order; Laurus consent order; Zydus consent order; In re: Entresto (Sacubitril/Valsartan) Patent Litigation, DDE-1-20-md-02930, Dkt. Entry 1255 (Feb. 7, 2024) (Alembic sealed consent order). The ability to launch a generic product now is an advantage that only MSN enjoys based on the unique approval

pathway it has pursued.

This advantage for MSN is considerable. Given the $3 billion in U.S. sales reported for Entresto in 2023, MSN could potentially realize revenue worth tens of millions of dollars every week that it is the sole generic entrant on the market. Novartis relies on Grabowski when asserting that "[i]t is well known in the pharmaceutical industry that generic drugs quickly replace branded products in the marketplace soon after their launch." Dkt. No. 3-1 at 12. As reported by Grabowski and discussed above, market penetration for generics in the first month after first generic entry is closer to 50%, not the 85-90% argued by Novartis. *See* Grabowski, et al., Fig. 5; Dkt. No. 3-1 at 26. Even using Grabowski's more modest generic market penetration percentage, if MSN were to launch as the sole generic entrant on the market, it could earn tens of millions of dollars during the first few weeks on the market.

It is customary in the pharmaceutical industry, however, for settlement agreements to include acceleration clauses allowing the settling generic party to launch upon an at-risk launch by another party. Assuming that they have such a provision in their settlement agreements, Alembic, Crystal, Zydus, and Laurus may be preparing for an accelerated launch (triggered by an MSN launch at-risk) at this very moment, meaning that every day that MSN is prevented from entering the market is a day closer to which these other generic companies may be ready to launch their products. Thus, if the TRO is entered and these other generic companies, which have final approval, are able to complete their launch preparations while the TRO is in place, MSN may be completely stripped of any advantage of being the first and sole generic entrant.

In fact, data from FDA shows that prices of generic drugs for a given brand product continue to decline as additional generic drug products enter the market. The FDA has reported that the average generic drug price is 39% less than the brand price if there is only a single generic

product on the market. Ryan Conrad, et al., *Estimating Cost Savings from New Generic Drug Approvals in 2018, 2019, and 2020*, at 4 (Aug. 2022) https://www.fda.gov/media/161540/download (last visited August 5, 2024); Ryan Conrad, et al., *Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition and Lower Drug Prices*, at 2-3, 9 (December 2019) https://www.fda.gov/media/133509/download (last visited August 5, 2024). As additional generic drugs enter the market, however, the prices for generic products precipitously decline. In fact, FDA reports that, on average, the price of generic drugs decreases to 79% below the cost of the brand product when there are four generic products on the market, and plummets to 95% below the cost of the brand product when there are six generic products on the market. *Id*. MSN should be rewarded for its efforts in obtaining FDA approval and creating the first pathway to market for a generic product, but the entry of a TRO delaying MSN's market entry would strip MSN of that reward given the drastic adverse impact a delay may have on MSN's price and revenue. This additional financial incentive for MSN is temporary, and may be short-lived, but is nonetheless a benefit MSN has earned in view of its unique approach to approval.

Courts have recognized that "the earliest generic drug manufacturer in a specific market has a distinct advantage over later entrants." *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 (D.C. Cir. 1998). This advantage is significant because it "can never be fully recouped through money damages or by 'playing catch-up.'" *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 29 (D.D.C. 1997). If the TRO is granted, each of the other four approved first applicants will have additional time to prepare for launch based on the possibility of an MSN at-risk launch, which is likely a known possibility given Novartis' TRO Motion.

Thus, the balance of hardships does not favor Novartis. Whatever hardship Novartis may have identified (based on inflated financial projections and inaccurate assumptions regarding time

on the market and market erosion), Novartis has not demonstrated that this hardship outweighs the harm that MSN would suffer by being deprived of the ability to be the first and sole generic entrant in the Entresto generic market.

In addressing the balance of equities, courts consider whether an injunction would "substantially injure other interested parties." *McGinn, Smith & Co., Inc. v. Fin. Indus. Regulatory Auth.*, 786 F. Supp. 2d 139, 144 (D.D.C. 2011) (quoting *Chaplaincy of Full Gospel Churches v. England,* 454 F.3d 290, 297 (D.C. Cir. 2006)); *see Winter v. Natural Resources Defense Council, Inc.*, 555 U.S. 7, 24 (2008) ("courts 'must balance the competing claims of injury and must consider the effect on each party of the granting or withholding of the requested relief.'" (quoting *Amoco Prod. Co. v. Village of Gambell,* 480 U.S. 531, 542 (1987)). Here, MSN has demonstrated that it would suffer serious harm and significant financial loss were the Court to delay MSN from commercial marketing. MSN made substantial investments in anticipation of its market launch, including manufacturing, preparation of sales staff, and formulating market projections and a business plan for the launch of its generic sacubitril/valsartan product. The value of these investments will be substantially lost if the Court grants a TRO and enjoins FDA's approval of MSN's ANDA.

D. A TRO would be contrary to public interest.

Granting Novartis' motion for a TRO will also not further the public interest. Rather, by permitting MSN to open the generic market for sacubitril/valsartan, the public interest will be served.

Generic competition for Entresto will significantly lower prices for vulnerable patients and payors. *See Illinois Tool Works, Inc. v. Grip-Pak, Inc.*, 906 F.2d 679, 684 (Fed. Cir. 1990) (recognizing "a public interest in the protection of patent rights," but deeming that interest counterbalanced by a competitor's "continuing right to compete"); Ex. A, Engilman, et. al.,

Estimated Medicare Part D Savings From Generic Drugs With a Skinny Label, Annals of Internal Medicine, Vol.177:6 (April 30, (2024) (demonstrating skinny label generic competition has resulted in billions of dollars saved through the Medicare Part D Program). Thus, the availability of generic sacubitril/valsartan further serves the public interest by providing consumers increased access to cheaper, safe generic drugs.

The FDCA is structured to give incentives to companies to file ANDAs so that lower-cost generic drugs are brought to market as soon as possible. "[T]he public has an interest in receiving the benefit of ANDA-approved generic drugs as soon as those products can lawfully come to market." *Pharmacia & Upjohn Co. v. Ranbaxy Pharms. Inc.*, 274 F. Supp. 2d 597, 614 (D.N.J. 2003), aff'd in relevant part, 85 F. App'x 205 (Fed. Cir. 2003). The Hatch-Waxman Act was implemented "'to speed the introduction of low-cost generic drugs to market,' thus increasing competition and, theoretically, lowering prices." *Id*. (quoting *Caraco Pharm. Labs., Ltd. v. Novo Nordisk A/S*, 566 U.S. 399, 405 (2012)) (internal citations omitted).

Having MSN's generic on the market sooner, rather than being erroneously delayed, will lead to lower prices for patients and payors, which will benefit the public and satisfy the intent of the FDCA. Data from FDA generally shows that prices for a drug can drop by as much as 75% within a year of the first generic approval and market entry, and for products with as little as a single generic drug competitor, the average drug price is 39% lower than the brand drug price prior to generic competition. Ryan Conrad, *Estimating Cost Savings*, at 4; Ryan Conrad, *Generic Competition and Drug Prices*, at 2-3, 9. For a product like Entresto, with reported U.S. sales of $3 billion in 2023 (i.e., roughly $250 million per month), the savings provided to patients who need this medication would be enormous.

In passing the Hatch-Waxman Act, "Congress sought to get generic drugs into the hands

of patients at reasonable prices – fast." *In re Barr Labs., Inc.*, 930 F.2d 72 (D.C. Cir. 1991). Brand companies' attempts to prolong their exclusivity in the market and prevent generic launch has been rejected by this Court and others. *See Hill Dermaceuticals, Inc. v. FDA*, 826 F. Supp. 2d 252, 262 (D.D.C. 2011) ("FDA is mandated by the FDCA to make lower-cost generic drugs available to the public where, as here, those drugs are found to meet the requirements for approval. It is therefore not in the public interest for the Court to grant a preliminary injunction preventing these generic drugs from being sold on the market."); *Biovail Corp. v. FDA*, 519 F. Supp. 2d 39, 50 (D.D.C. 2007) ("[T]he public also has a well-recognized interest in 'receiving generic competition to brand-name drugs as soon as is possible,' *Boehringer Ingelheim Corp. v. Shalala*, 993 F. Supp. 1, 3 (D.D.C. 1997), and a 'delay in the marketing of [the generic] drug could easily be against the public interest in reduced prices,' *Schering Corp. v. Sullivan*, 782 F. Supp. 645, 652 (D.D.C. 1992). As in *Biovail*, Novartis has not shown that the FDA misapplied the applicable statutes and regulations or that generic sacubitril/valsartan products are unsafe. Therefore, a TRO and the consequent delay of MSN's generic entry into the marketplace would not serve the public interest.

Notably, the cost for a monthly supply of Entresto's 24-26 mg oral tablets has been reported to be approximately $734 – an exorbitant figure. *See Entresto Prices, Coupons, Copay Cards & Patient Assistance*. Drugs.com. https://www.drugs.com/price-guide/entresto#:~:text=The%20cost%20for%20Entresto%20(24,accepted%20at%20most%20U.S.%20pharmacies;%20https://www.drugs.com/medical-answers/entresto-cost-month-3544065/#:~:text=Official%20answer&text=If%20you%20are%20paying%20cash,%2410%20using%20a%20copay%20card. Indeed, Novartis is known to market some of the most expensive drug products on the market. *See* Hannah McQueen, *The 10 Most Expensive Drugs in the US, Period*, GOODRX HEALTH, https://www.goodrx.com/drugs/savings/most-expensive-drugs-in-

us?label_override=undefined (Novartis' Zolgensma listed as the most expensive drug in 2022 with a one-time cost of $2.1 million for a course of treatment); Fraiser Kansteiner et al., *Most Expensive Drugs in the US in 2023*, FIERCE PHARMA, https://www.fiercepharma.com/special-reports/priciest-drugs-2023 (Novartis' established gene therapy Zolgensma continues to orbit the top of the U.S. price rankings for 2023). Safeguarding and encouraging fair competition in pharmaceutical markets is highly advantageous for the American public, especially when prices are unreasonably inflated due to limited or nonexistent competition. Comment of the U.S. Federal Trade Commission, at 5-7 (Feb. 6, 2024). Ultimately, the public interest weighs in favor of denying Novartis' requested TRO.

V. CONCLUSION

For all the above reasons, Intervenor-Defendants respectfully submit that Novartis' TRO Motion should be denied.

Dated: August 6, 2024

Respectfully submitted,

POLSINELLI PC

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CERTIFICATE OF SERVICE

This is to certify that on August 6, 2024, I served the foregoing with the Clerk of the Court using the CM/ECF System, which will send electronic notification of such filing to all counsel of record.

/s/ Chad Landmon
Attorney for MSN Pharmaceuticals Inc. and MSN Laboratories Private Limited